THE SURGICAL CLINICS OF NORTH AMERICA

APRIL 1976

PEDIATRIC SURGERY

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THE SURGICAL CLINICS OF NORTH AMERICA

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SYMPOSIUM ON
PEDIATRIC SURGERY

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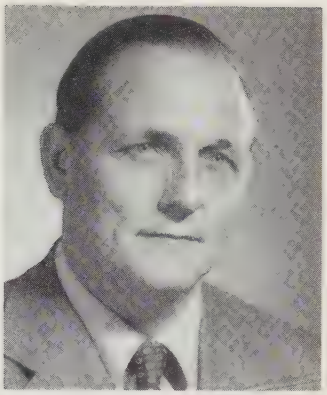

FABIAN BACHRACH

Foreword

Pediatric surgery was the subject of an issue of *Surgical Clinics of North America* first in 1956, edited by Dr. Willis J. Potts, and again in 1964 with Dr. Orvar Swenson. There have been many changes in the field since then, both in the care of surgical conditions which affect infants and children and also in the recognition of pediatric surgery as a specialty. In the American Academy of Pediatrics there are sections of Pediatric Surgery, Pediatric Urology, and Pediatric Anesthesiology, whose members devote all or most of their time to caring for children. Publication of the *Journal of Pediatric Surgery* began in 1966. The American Pediatric Surgical Association was founded in 1970. The American Board of Surgery gave its first examination in 1975 for certification of competence in Pediatric Surgery. Hopefully this example may be followed by other surgical disciplines. All of the above underscores that care of children is the principal activity of many surgeons today. Clearly, results of surgery for major malformations are best in the hands of those who deal with children regularly.

An issue of *Surgical Clinics* cannot cover completely a field which has grown so large in scope. In this volume are omitted the many common things familiar to most general surgeons, i.e., appendicitis, hernia, intussusception, etc. Instead, in general, I have selected topics in which treatment has changed greatly in recent years. The invited authors, from a broad spectrum of institutions, present their own current concepts of what can be achieved in treating certain disorders. It is my hope that the readers will welcome this update in selected areas. Some of the topics are highly specialized, to be sure, but a surgeon who treats imperforate anus should know what the cardiac surgeon can accomplish if the infant has congenital heart disease as well. Most of the topics are pertinent to the everyday practice of surgery of infants and children.

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Physiologic Considerations in the Newborn Surgical Patient

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and Michael B. Marchildon, M.D.†

We have chosen six aspects of newborn physiology—the birth weight gestational relationship, glucose metabolism, temperature regulation, calcium balance, infection, and fluid and electrolyte balance—as examples of important considerations that must be understood to successfully manage the newborn surgical patient. Equally important subjects such as cardiovascular, pulmonary, and renal function, because of space limitation, will not be discussed. It is our hope that this article, although incomplete, will serve as an introduction and stimulus to the further study of the still undeveloped field of newborn surgical physiology.

LOW BIRTH WEIGHT INFANTS

With the development of concepts of fetal malnutrition,[34] the establishments of standards of intrauterine growth,[50] and the availability of techniques to assess gestational age on the basis of neurologic development,[4, 44, 67] it became apparent that all newborn babies below 2500 gm were not prematurely born. Many were low in weight as a result of intrauterine malnutrition, infection, inherited factors, or congenital abnormalities. It has been estimated that one third of all babies less than 2500 gm are actually full-term babies that are small for gestational age. The incidence of small for date infants with major surgical problems is not known. However, Cozzi and Wilkinson[17] recently found that of 142 patients with esophageal atresia and tracheoesophageal fistula, 56 were below 2500 gm in weight. Fifty-two per cent of the small babies were prematurely born while 48 per cent were small for gestational age and full-term. Since preterm and small for gestational age infants face dif-

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Table 1. *Surgeon's Assessment of Low Birth Weight Baby*

CHARACTERISTIC	PRETERM BABY	TERM SMALL FOR GESTATIONAL AGE BABY
SKIN		
Texture	Very thin, gelatinous, transparent	Smooth, medium thickness, rash or peeling especially of hands and feet
Color	Dark red	Pale; pink over ears, lips, palms or soles
Plantar creases	No creases or faint red marks	Distinct; complete and multiple
EARS	Soft, malleable with poorly developed cartilage	Cartilage well developed; ears firm, instant recoil
BREASTS	Nipple barely visible; no areola; no palpable tissue	Well developed areola and nipples; breast tissue both sides
GENITALIA		
Male	Undescended testicles; poorly developed scrotum	Testes fully descended; scrotum fully developed; good rugae
Female	Large labia minora; labia majora widely separated	Labia majora completely over labia minora

ferent physiologic problems, it is essential that the surgeon accurately categorize low birth weight babies as: preterm, less than 37 weeks, or term, 37 through 42 weeks gestation, appropriate in weight for gestational age, or small for gestational age. The assessment of gestational age of an individual baby can be most accurately done by scoring systems.[23] However, a rough determination can be made by the body weight, the historical information of pregnancy and a few physical characteristics (Table 1).

Small for gestational age babies have a high incidence of pulmonary aspiration of meconium and amniotic fluid. Pneumonia is more common in the postoperative small for date baby.[17] The preterm infant more frequently has poorly developed lungs, an immature surfactant system, and a markedly increased incidence of hyaline membrane disease. Neonatal hypoglycemia is more often encountered in babies that are small for gestational age. Small for date infants have adequate serum calcium levels at birth while preterm infants often have low levels and more frequently suffer from tetany. Infants who are small for gestational age frequently have hematocrits over 60 per cent. Blood viscosity is markedly increased as hematocrit rises to levels above 70 per cent; this can lead to poor tissue perfusion and signs of congestive heart failure. When high values are encountered, blood letting and replacement by plasma should be considered. Metabolic rate is higher in small for gestational age babies than preterm babies of similar weight. This difference is particularly prominent by the second and third day of life.[40, 46] Preterm babies below 1500 gm appear to be particularly vulnerable to water deficits because of high insensible water loss.[25] The elevated insensible water loss is probably due to skin factors, particularly the large surface

area in relationship to body weight, and thinner epidermis, greater skin permeability, and more superficial blood supply to the skin.[31, 57, 71, 89]

GLUCOSE METABOLISM

Neonatal hypoglycemia is a common physiologic derangement that can produce irreversible neurologic damage if not promptly diagnosed and treated. As term approaches, increasing amounts of glycogen are stored in the liver and heart muscle. At birth rapid glycogenolysis occurs, depleting the stored glycogen in the first few hours of life. As this source of stored energy is consumed, gluconeogenesis assumes a vital role as a mechanism of maintaining blood glucose levels. Hypoglycemia can result from inadequate delivery of substrate to the liver or from deficiency in the gluconeogenic pathways. Any derangement in the metabolic sequence of gluconeogenesis can result in hypoglycemia soon after birth. The other major mechanism for hypoglycemia is an increase in circulating insulin levels.[55]

Hypoglycemia can be defined, chemically, as a blood glucose level below 30 mg per 100 ml in full-term infants or below 20 mg per 100 ml in low birth weight infants during the first 3 days of life. Symptomatic hypoglycemia causes such signs as jitteriness, cyanosis, apnea, lethargy, hypotonia, or seizures, which respond to the administration of intravenous glucose. These signs are nonspecific and a wide differential diagnosis must be entertained.

The highest risk groups are small for gestational age babies (SGA), particularly when also preterm, and infants of diabetic mothers. Chemical hypoglycemia in the first few hours of life may occur in up to 40 per cent of SGA babies, while symptoms responsive to glucose administration occur in about 6 per cent.[49, 58] In SGA babies the etiology of the hypoglycemia appears complex. In addition to inadequate gluconeogenesis, decreased hepatic glycogen stores, possibly on the basis of fetal malnutrition, and increased circulating insulin levels may be of significance in some babies.[47] Preterm infants have an increased incidence of hypoglycemia but far less than babies who are SGA. Fifty per cent of infants of diabetic mothers become hypoglycemic, and these babies generally have increased levels of circulating insulin. Birth hypoxia and maternal toxemia of pregnancy also increase the risk of hypoglycemia in the newborn.[27]

Routine Dextrostix (Ames) determination in the first few hours of life should be performed in all high risk babies and followed closely. Babies with low Destrostix values or possible symptoms should have serum glucose determinations. The presence of symptoms is an indication for rapid treatment, since neurologic damage has been reported in 30 to 50 per cent of symptomatic babies.[45, 58] This figure is vastly reduced in vigorously treated infants. Stern[76] advised correction of all blood glucose levels below 40 mg per 100 ml, since the limits for risk of brain damage are not known. Treatment consists of an immediate intravenous infusion of 50 per cent dextrose in water at 1 to 2 ml per kg body weight, followed by maintenance infusion of 10 to 15 per cent dex-

trose at 75 to 85 ml per kg per 24 hours. Glucose infusions must be tapered slowly to avoid rebound hypoglycemia.[86] Corticosteroids[86] have been suggested as adjunctive therapy, though no critical studies of the results of this treatment have been reported. Glucagon should never be used alone as therapy because the clinical response is variable.[48]

TEMPERATURE REGULATION

The baby at birth is a thermically active individual who has a specific environmental temperature which represents thermal neutrality. At this ambient temperature the metabolic activity and resulting heat production are at a minimal or basal level. When environmental temperature falls below the thermal neutral zone, metabolic activity increases and heat production rises in an attempt to maintain a normal body temperature in spite of the cold environment.[38, 39] A healthy full-term infant can respond to a brief cold exposure by an almost threefold increase in metabolic activity and maintain a normal body temperature.[11] Premature babies show the same thermal response as full-term infants, but their response is qualitatively below the term baby. The small for gestational infant, despite his small size, has a well developed homeothermic response closely resembling the full-size baby.[74]

Although infants have a well developed temperature regulating system, they are at a disadvantage in comparison to the adult when faced with a cold environment because the babies' tissue insulation is low and varies with body weight and fatness, and because all babies have a relatively large surface area in relation to body mass. Continued cold exposure is detrimental to the infant because the increased metabolic work necessary to maintain normal body temperature results in exhaustion of body stores, an increase in metabolic breakdown products, and an accelerated insensible water loss.[29] As cold exposure continues and the metabolic activity cannot produce adequate heat, body temperature falls. The baby becomes hypothermic, has a low body temperature and a metabolic debt.

The ideal physical environment to maintain a newborn infant would provide an ambient temperature at thermal neutrality and have an absence of cool surfaces to which the baby may radiate heat. Statistical tables[35, 69] have been created to take into consideration such factors as gestational age and size to calculate the neutral thermal zone. These give a rough guide and are helpful. An effective approach to minimize heat production is to regulate skin temperature. Oxygen consumption is minimal when the abdominal skin temperature is approximately 36.2° C in the full-term infant and 36.5° C in the low birth weight baby.[12, 72] Proper skin temperature can be maintained automatically by adding a servomechanism to an incubator or heat panel. If the skin temperature drops below the set level, heat output increases until the desired skin temperature is reached. Combining simultaneous measurements of rectal and skin temperature is an excellent indicator of metabolic work and heat production. The gradient between rectal and skin temperature should be less than 1.5° C[2] if metabolic activity is minimal. An increase

in the gradient suggests that metabolic activity and heat production have increased in order to maintain the body temperature at a normal level.

The common practice of monitoring rectal temperature alone as a method of preventing increased heat production is not physiologically sound. In a cold environment it is possible for an infant to maintain normal rectal temperature by maximally responding with thermogenesis. A normal body temperature as measured by rectal thermometer is not evidence that metabolic activity is basal.

To summarize: when an infant is placed in a cool environment that is below the thermal neutral zone of that particular infant, he responds with increased metabolic work and heat production. More calories are expended in order to keep warm and fewer calories become available for growth and response to disease and operation. Energy reserves are depleted and insensible water loss increases. Metabolic breakdown products accumulate and metabolic acidosis develops. To minimize thermal stress, the environmental temperature in which the baby is maintained should be kept close to the infant's thermal neutral zone and the surfaces that cause radiant heat loss should be minimized. Skin and rectal temperature should be monitored.

CALCIUM BALANCE

The newborn infant, particularly the premature baby, may develop hypocalcemia in the first days of life. The preterm infant is specifically at risk since over 75 per cent of calcium transport across the placenta occurs after the 28th week of gestation. An important contributing factor is the immaturity of the endocrine system. The preterm baby often produces inadequate amounts of parathormone in the first days of life.[24, 83, 84] In contrast, infants that are small for gestational age but term, and full-sized, term babies have a placental transport mechanism that is able to supply normal calcium stores by birth and a relatively mature endocrine system.

Iatrogenic factors add to the risk of hypocalcemia in all babies. Administration of sodium bicarbonate to correct acidosis decreases the ionized fraction of calcium and can produce clinical symptoms. Exchange transfusions with citrated blood complex both calcium and magnesium and lower serum concentration precipitously.

The vast majority of infants who develop hypocalcemia do so in the first 48 hours of life. Full-term infants are born with calcium levels 1 mg per 100 ml higher than maternal levels due to active placental transfer. These levels then fall slowly to an average minimal value of 9.0 mg per 100 ml at 48 hours.[63] As parathormone production increases, the levels rise to normal again over the next few days. Chemical hypocalcemia is defined as a serum calcium below 7.5 mg per cent and occurs in about 1 per cent of all births. True hypocalcemic tetany occurs in only about 0.1 per cent.[68]

There are four high risk groups: true preterm babies, infants of diabetic mothers, stressed infants, and babies receiving bicarbonate in-

Table 2. *High Risk Groups for Hypocalcemia*

INFANT GROUPS	MECHANISMS OF HYPOCALCEMIA
True preterms	Inadequate calcium stores Insufficient parathormone production
Infants of diabetic mothers (25-fold increased risk)	Inadequate parathormone production[8]
Infants with low Apgar scores; stressed infants up to 39 per cent affected[62]	Endogenous corticosteroid production, lowering calcium levels and stimulating calcitonin release, further decreasing serum calcium
Infants receiving bicarbonate infusions or exchange transfusions	Decrease in plasma fraction of ionized calcium

fusions or exchange transfusions (Table 2). Many surgical patients fall into these categories. Serum calcium levels should be drawn following major surgical procedures in the first few days of life, in all preterm infants, and routinely following administration of sodium bicarbonate or exchange transfusions.

The appearance of hypocalcemic symptoms after 1 week of age is far less common and related to oral feedings. Symptoms occur in babies fed cow's milk formulas which have high phosphate levels. The kidneys of the newborn baby are unable to excrete the large phosphate load and the serum calcium level is driven downward. About 50 per cent of the infants who develop late hypocalcemia also have one or more of the high risk factors. Breast milk and commercial formulas that are relatively low in phosphate content should be used instead of cow's milk formula in the high risk groups of infants.

As in the case of hypoglycemia, the symptoms of hypocalcemia are nonspecific. Jitteriness, twitching, and seizures are most common, but cyanosis and vomiting can also occur.[68] Increased muscle tone is generally seen with hypocalcemia, whereas hypotonia is associated with hypoglycemia. Evaluation of a "jittery baby," whether pre- or postoperative, consists of Dextrostix, blood glucose, and serum calcium determinations. Convulsions associated with hypocalcemia, as opposed to hypoglycemia have a good long-term prognosis.[15]

Only in the presence of seizures or extreme irritability should parenteral calcium be administered.[86] In acute situations 10 per cent calcium gluconate is injected slowly (1 ml per min) into an intravenous line, with continuous monitoring of the electrocardiogram or apical pulse. The maximal dose is 10 ml for a full term and 6 ml for a premature infant.[56] For maintenance therapy when oral calcium cannot be administered, e.g., postoperatively, 10 per cent calcium gluconate can be continuously infused at 10 to 20 ml per 24 hours. Intravenous calcium is rarely required for more than 24 to 48 hours. Great care must be taken to avoid extravasation of calcium solutions because of the danger of skin necrosis.

Oral calcium therapy is the treatment of choice for asymptomatic hypocalcemia. Calcium chloride is probably the most effective agent but may cause gastric irritation or metabolic acidosis. Calcium lactate, calcium gluconate, and calcium glubionate are alternative preparations administered at 2 to 4 mg per day. Therapy is usually tapered after 2 to 4 weeks. Low phosphate formulas may also be of benefit.

INFECTION

Overwhelming infection is an often fatal complication threatening the newborn surgical patient. There are multiple factors contributing to the apparent increased frequency of infection. Deficiencies in the newborn immune defense mechanisms appear to be a prime factor. For this reason a basic understanding of immunocompetence is important for the surgeon. The immune mechanisms can be categorized as (1) antibody-mediated immunity, (2) cell-mediated immunity, (3) phagocytosis, and (4) complement.

Antibody Mediated Immunity

Circulating B lymphocytes and tissue plasma cells produce immunoglobulins. This production begins in utero at 10½ weeks of gestation[30] but is still minimal at birth. The major immunoglobulin classes IgG, IgM, and IgA have a common basic structure but are very different in their rate of development and in their ultimate role in the immune system. Some physical properties of these immunoglobulins are listed in Table 3.[5, 78]

IgG is unique from the other immunoglobulins in that it alone crosses the placenta, largely in the last trimester. Serum concentration of IgG are directly related to gestational age.[41] Full-term babies have near adult levels at birth, virtually all of which is maternal in origin. Maternal IgG gradually disappears in the first few months after birth, as the baby's own IgG production increases. IgG is active primarily against gram-positive organisms, yet these infections are common in the newborn. This suggests that the passive protection derived from the mother is incomplete and that active immunity is more effective.

Table 3. *Properties of Immunoglobulins*

	IgG	IgM	IgA
Molecular weight	150,000	900,000	170,000 (serum) 370,000 (secretory)
Mean newborn concentration mg per 100 ml	1000	11	2
Mean adult concentration mg per 100 ml	1200	100	200
Placental transfer	+	0	0
Binds complement	+	+	0
Half-life (days)	26	5	7

IgM antibodies are the major antibodies directed at gram-negative organisms. The low IgM levels at birth may in part account for the newborn's susceptibility to gram-negative infections. Elevation of IgM suggests exposure to intrauterine infection, e.g., rubella, syphilis, etc., and is used as a diagnostic aid in suspected cases.

IgA exists as a monomer form in serum and a dimer form in secretions. Secretory IgA and phagocytic cells are found in high concentrations in breast milk, and these may have a protective effect on the gastrointestinal tract of breast-fed newborns.[7, 59, 87]

Though serum levels of immunoglobulin are important, the resistance of the newborn infant to infection depends on his ability to respond to a challenge by increased production of specific antibody. In many situations the antibody response appears satisfactory.[3] Small for gestational age infants (SGA), however, may have diminished capacities when challenged.[13]

Cell Mediated Immunity

The cellular immune system is comprised of T lymphocytes in the circulation, lymph nodes, and spleen. This system is protective against viral, fungal, and protozoal infections, as well as malignancies and graft vs. host reactions.[77] Cellular immunity may function in utero to eliminate maternal lymphocytes that leak across the placenta, preventing a graft vs. host reaction. Some babies infected with rubella in utero shed no virus when born, suggesting a functioning cellular immunity system. Most neonates, however, do not appear to have mature cellular immunity. Full-term, preterm, and SGA babies respond weakly and inconsistently to skin testing with DNCB,[85] and SGA infants have markedly decreased peripheral T-lymphocytes.[13]

Phagocytosis

The complex process of phagocytosis can be subdivided into four phases: chemotaxis, opsonization, ingestion of the agent, and intracellular killing (bactericidal capacity). Studies have been performed on the circulating phagocytes, the neutrophils, but not on tissue phagocytes, the macrophages.

CHEMOTAXIS. Newborn polymorphonuclear leukocytes (PMN's) appear to have decreased random motility and a diminished movement toward chemotactic agents.[13, 61] This may be of importance in the poor ability of the newborn to localize infections.[21]

OPSONIZATION. The interraction of a foreign substance with serum proteins, opsonization, is a prerequisite to phagocytosis. Newborn serum is deficient in opsonic factors, particularly for gram-negative organisms.[22, 54] This deficiency may be attributable to reduced newborn levels of complement or, possibly, IgM.

PARTICLE INGESTION. In healthy full-term, preterm, or SGA infants, bacterial ingestion is normal if opsonization is adequate.[13, 52] In sick or stressed infants, phagocytic ingestion may be impaired, especially for gram-negative organisms.[28, 91]

BACTERICIDAL CAPACITY. Most studies on full-term newborns

suggest normal killing capability of leukocytes, except possibly in the first 12 hours after birth.[16] The bactericidal capacity of healthy preterm or SGA infants is disputed.[13, 28] In stressed or septic newborns or in malnourished children there appears to be deficient bactericidal capacity for both gram-positive and gram-negative organisms.[6, 14, 70, 91]

Complement. Complement (C′) refers to nine serum factors in the globulin fraction which act sequentially to amplify the effects of all three of the immunologic systems previously discussed. Complement binds IgG and IgM, is synthesized very early in utero, but does not cross the placenta. Complement levels at birth are directly correlated with gestational age[26] and reach 50 to 65 per cent of maternal levels in full-term infants. As complement plays a key role in opsonization and in the release of chemotactic factors, the decreased newborn complement levels may be largely responsible for the defects observed in these mechanisms.

In summary,[21] the newborn immune response is characterized by normal IgG levels which are maternal in origin, low IgM and complement levels, deficient opsonic activity, a decreased inflammatory response by neutrophils, and poorly developed cell-mediated immunity. In addition, these functional deficits are magnified and new deficiencies appear in stressed or septic infants, and to a lesser extent in preterm and SGA infants.

Although the reduced defense against infection appears to play a major role in the prevalence of newborn infections, there are many other contributing factors that must be considered. The infant may be exposed to infecting agents before birth. Infection of the fetus with virus or protozoa by the transplacental route is relatively common,[10] although bacterial infection by the route is far less frequent.[42, 88] Ascending infection resulting in chorioamnionitis is more common and is found in 7 to 15 per cent of all births.[32] The incidence rises to 20 per cent in cases where membranes rupture more than 24 hours antepartum.[9] Although contamination and amnionitis are common, systemic infection, particularly pneumonia, occurs in only 1 to 3 per cent of babies with infected amnionic fluid.[10]

Recent advances in perinatal medicine, particularly more effective respiratory, nutritional, and blood incompatibility management, may contribute to the prevalence of newborn infection by making possible the survival of a large population of small, debilitated, and susceptible infants. In addition, improved management of the newborn has brought iatrogenic dangers. The widespread use of intravascular catheters for monitoring and total intravenous nutrition has increased the risk of bloodstream contamination. Endotracheal tubes and nasogastric and urinary catheters are commonly used to manage the sick baby. They increase the exposure of the infant to pathogenic bacteria. Gram-negative organisms flourish in water and moisture. Sinks, incubators, and inhalation therapy equipment serve as an important reservoir of bacteria that can contaminate the baby.

The common practice of administering multiple antibiotics to high-risk patients has led to the emergence of resistant bacterial strains in

many newborn centers. Large regional neonatal centers place many infants suffering from a variety of septic and nonseptic conditions into one large unit. This allows multiple opportunities for cross contamination. Constant physical contacts between the baby and the medical personnel are commonplace. Teams of doctors, nurses, students, technicians, maintenance men, and geneticists repeatedly handle the infant and his equipment; they make breaks in technique a daily occurrence.

Management

Obviously every effort should be made to prevent infection. Traffic flow in neonatal units should be controlled. Exposures of the patient to multiple personnel should be limited and strictly monitored. Isolation procedures must be enforced. Indwelling catheters should be inserted only when there is a clear-cut indication, managed with meticulous technique when in place, and removed as quickly as possible. The indiscriminate use of multiple antibiotics because of the fear of infection should be guarded against.

The early diagnosis of newborn infection and prompt therapy before major pathologic changes occur offers the best chance for survival of the afflicted infant. Subtle changes in clinical signs are usually the first clues to infection. A fall in body temperature, poor feeding, reduction in activity, abdominal distention, or an increase in apnea episodes should immediately suggest sepsis. A thorough physical examination and cultures of the nose, throat, umbilicus, stool, and wound are then taken. Multiple blood samples for aerobic and anaerobic cultures are drawn. Urine for analysis and culture can be obtained by a clean catch collection or by a suprapubic stick. As meningitis is reported in up to 33 per cent of infants with neonatal septicemia,[32] lumbar puncture is essential. More than a few PMN cells and a total cell count of over 10 is considered strong suggestive evidence of meningitis. A white blood cell and differential count is usually not helpful although a low white blood cell count suggests gram-negative septicemia.[33, 93] We have found that serial measurements of the platelet count is a rapid and helpful method for the early detection of gram-negative septicemia. Infants with a positive blood culture for gram-negative organisms have platelet counts generally below 150,000 and in 71 per cent of cases the count is below 100,000. It is our feeling that, if the platelet count falls below 150,000, this is strong presumptive evidence of gram-negative septicemia and if even minimal clinical signs of infection are present, treatment should be initiated.[64]

Since newborn septicemia can be rapidly devastating, antibiotic therapy should be initiated in suspected cases before culture reports are available. Antibiotics can be discontinued in 48 to 72 hours if all cultures are negative and the infant appears clinically well. A combination of antibiotics is usually utilized to provide broad-spectrum coverage and for potential synergistic effect.[18, 43] The choice of antibiotics when culture and sensitivity reports are not available is based on clinical suspicion and the prevalent organisms in the nursery. The flora in a given nursery is dependent on the antibiotic agents which have been most fre-

quently used. A knowledge of the current pathogens encountered and their antibiotic sensitivity is essential in planning therapy.[1, 20]

Transfusions and exchange transfusions with fresh adult blood may be beneficial in cases of serious neonatal septicemia, particularly when there is evidence of disseminated intravascular coagulation. The blood used must be fresh, because stored blood loses its bacteriocidal activity completely after 4 days.[53] It is not clear whether the efficacy of fresh adult blood is due to the white blood cell or platelet fractions, opsonins, or IgM.[19]

FLUID AND ELECTROLYTE BALANCE

Maintenance fluid and electrolyte requirements of the newborn surgical patient are related to total metabolic activity—the rate the baby turns over water, electrolytes, and substrate—rather than to body weight. The meter square method utilizes the theoretic relationship between metabolic rate and body surface area to calculate maintenance water and solute requirements.[66] Total water requirements with this method is calculated as 1200 to 1500 ml per M^2 per 24 hr. Daily sodium and potassium needs are similarly calculated as 40 mEq per M^2 per 24 hr and 30 mEq per M^2 per 24 hr, respectively.[80-82] Sinclair et al.,[75] Hill and Robinson,[40] and Winters[90] challenged the accuracy of the relationship between body surface area and metabolic activity. As doubts were raised as to the validity of the meter square method, the caloric method of calculating fluid and electrolyte needs became more popular. This system appeared to be "physiologically more appropriate."

The caloric method employs a nomogram or formula utilizing both weight and age to calculate energy expenditures. For the newborn infant many clinicians simply use the figure of 75 calories per kilogram per 24 hours. Employing the fixed figure or the nomogram, total water maintenance is determined by assuming that 100 ml of fluid are utilized per 100 calories metabolized per 24 hr. Maintenance electrolyte requirements are figured on a similar basis with sodium and potassium 1 to 3 mEq per 100 calories per 24 hr.[90]

Although both the meter square and the caloric methods superficially appear to be based on metabolic activity, they are actually indirect systems that estimate metabolic rate based on variables such as age, weight, and body length. These systems, although helpful, cannot be completely relied upon because metabolic rate and insensible water loss are dependent on many factors and no nomogram or formula can accurately estimate them for the individual newborn patient. The energy expended varies with gestational age, ambient temperature, radiant surfaces the baby is exposed to, humidity, and the infant's activity and feeding pattern.[36, 73] Changes in the respiratory rate and duration of crying can increase insensible water loss significantly.[37, 94] Babies placed under a bilirubin light or cared for in a radiant heater[92] and the immature infant below 1500 gm have markedly increased insensible water loss.[25] To add to the difficulty the infant's internal environment is rap-

idly changing as a result of extrauterine adaptation and maturation. Total body water at birth is proportionally greater than in the adult and plasma and extracellular water is greater. Intracellular water increases as growth proceeds. Renal function in the newborn infant is characterized by a low sodium excretion, glomerular filtration rate, and urine concentrating ability. Even among healthy full-term infants, urinary flow rate, clearance, and the ability of the kidney to dilute urine vary from baby to baby.[79]

Since it is clear that formulas, systems, and rules of thumb cannot precisely determine the fluid needs of an individual infant suffering from a major surgical illness, how do we treat the infant who requires fluid and electrolyte therapy? We believe that proper management involves four steps: (1) The theoretic maintenance needs of the infant should be calculated utilizing one of the formulas. (2) When possible, losses should be directly measured and immeasurable losses estimated. (3) The fluid and electrolyte program should be initiated with a clear understanding that it is on a trial basis. (4) The infant's responses to the tentative program must be serially monitored—we must constantly "read the baby" and adjust the rate, total volume, and electrolyte content of fluids administered based on the information obtained by the monitoring.

We employ several methods to "read the baby." They include: clinical observation, body weight measurements, urine output, urine osmolality, hematocrit, refractometer total protein, serum electrolytes, and osmolality.

The activity of the infant, his skin turgor, and the condition of the fontanel are helpful guides to the state of hydration. One of the simplest and most helpful indications of total body water is serial measurement of body weight. Fluctuations in body weight over a 4 to 8 hour period are primarily the result of a loss or gain of body fluids. A loss or gain of 1 ml of total body water in the infant can be equated roughly to 1 gm of body weight lost or gained.

A newborn surgical patient receiving intravenous fluids produces about 400 to 600 ml of urine per M^2 per 24 hr or 50 to 70 ml per 100 calories metabolized per 24 hr. These estimates give the general range of what we should expect. Our main concern is the change in output as a result of fluid therapy. All newborn surgical patients should have careful urine output and measurements. In hypovolemic patients the urine volume should be measured hourly. If necessary a catheter or small feeding tube can be passed into the bladder for accurate and more frequent measurements.

The infant excretes a concentrated urine when dehydrated and a dilute urine when over hydrated. Urine osmolality, specific gravity, and refractory index are all relatively simple methods for evaluating the renal excretion of solutes and water and guide in the state of hydration of the baby. We prefer measuring urine osmolality, since it is a more direct measure of the number of particles in relation to the volume of the urine. The average value for urine osmolality in the newborn infant is 268 mOsm per kg; the range varies from 20 to 500 mOsm per kg. The

trend of serial measurements of urine osmolality rather than the individual values is most important in monitoring fluid therapy. Combining serial determinations of urine osmolality and volume provides a valuable guide to the quantity and rate of intravenous fluid to be administered.

Hematocrit is a measure of the ratio of red blood cell mass to plasma volume. Serial changes in hematocrit over an 8 to 24 hour period in the absence of hemolysis or bleeding suggests a loss or gain in plasma water. Total protein serially determined by a Goldberg refractometer, like the hematocrit, is a simple method of estimating plasma water. Over a 24-hour period, in the absence of massive protein loss, a fall in total protein suggests an increase in plasma water; a rise, a loss of plasma water.

The above methods are helpful in arriving at the proper volume of fluid to be administered. It is essential that electrolyte balance also be achieved and maintained. A rough estimate of the maintenance electrolyte requirements can be calculated by the meter square or caloric method. Electrolyte losses from sources such as the gastrointestinal tract can be determined by direct electrolyte analysis of samples. Pre-existing deficits and immeasurable losses must be estimated. Once the estimates of electrolyte maintenance and replacement have been determined, adjustments are made by serially monitoring serum electrolyte levels and osmolality.

Sodium, potassium and chloride can be measured on small samples in most clinical laboratories. When combined with the blood urea nitrogen and blood sugar, an excellent picture of the concentration of serum solutes to serum water is given. Serum osmolality gives less information than serum electrolyte determinations but has the advantage that only a small sample of serum is required and the measurement can be done rapidly by a physician or nurse rather than a trained technician. Osmolality is a measure of the concentration, the number of particles in a kilogram of solvent. In serum the sodium ion is the major determinant of osmolality. To a lesser degree blood sugar and blood urea nitrogen contribute to total osmolality.[51] Normal newborn serum osmolality is 270 to 280 mOsm per kg.[65]

Our approach to electrolyte therapy of a baby includes an initial measurement of serum electrolytes, blood urea nitrogen, sugar, and serum osmolality. The tonicity of the patient's serum is then followed during intravenous therapy by frequent determinations of serum osmolality. A rise in osmolality suggests that too little water or too great a quantity of electrolytes, usually sodium, has been given. A fall in osmolality suggests that sodium replacement is inadequate or that too great a quantity of water is being administered. An unexpected change in osmolality, particularly an increase, requires a repeat determination of serum electrolytes, blood urea nitrogen, and sugar.

To summarize: the volume of intravenous fluid is calculated by combining the information derived from formulas, measurements, and estimates. Orders are written for 4 to 8 hour periods. Clinical findings such as poor skin turgor, a sunken fontanel, a drop in body weight, a fall

in urine output and a rise in urine osmolality, hematocrit, and total protein suggest that the estimate of the quantity of fluid delivered to the baby is inadequate. The volume and rate of administration should be increased. Opposite changes suggest that too large a volume of fluid has been administered. Electrolyte maintenance is estimated by the use of formulas, and losses are both estimated and measured directly. The therapy is then monitored by serum electrolyte determinations and serial measurements of serum osmolality. Changes in the proportion of water to electrolytes are made on the basis of a fall or a rise in serum osmolality. Large changes in serum osmolality or unexplained changes require repeat electrolyte determinations.

REFERENCES

1. Ablow, R. C., Driscoll, S. G., et al.: A comparison of early onset group B streptococcal neonatal infection and the respiratory distress syndrome of the newborn. N. Eng. J. Med., *294*:65, 1976.
2. Adamsons, K., Jr.: The role of thermal factors in fetal and neonatal life. PED. CLIN. N. AM., *13*:599, 1966.
3. Adinolfi, M., and Wood, C. B. S.: Ontogenesis of immunoglobulins and components of complement in man. *In* Adinolfi, M., and Humphrey, J. (eds.): Immunology and Development (Clinics in Developmental Medicine No. 34). London, Heinemann, 1969, p. 27.
4. Amiel-Tison, C.: Neurological evaluation of the maturity of newborn infants. Arch. Dis. Child., *43*:89, 1968.
5. Ammann, A. M., and Wara, D. W.: Evaluation of infants and children with recurrent infection. Curr. Prob. Ped., *5*, Sept. 1975.
6. Anderson, D. C., Pickering, L. K., and Feigin, R. D.: Leukocyte function in normal and infected neonates. J. Pediat., *85*:420, 1974.
7. Beer, A. E.: Immunologic benefits and hazards of milk in the maternal-perinatal relationship: Natural transplantation of leukocytes during suckling. *In* Necrotizing Enterocolitis in the Newborn Infant. 68th Ross Conference on Pediatric Research, Aug. 1975, p. 48.
8. Bergman, L., Kjellner, I., and Selstrom, U.: Calcitonin and parathyroid hormone relation to early neonatal hypocalcaemia in infants of diabetic mothers. Biol. Neonat., *24*:151, 1974.
9. Blanc, W. A.: Amniotic infection syndrome: Pathogenesis, morphology, and significance in circumnatal mortality. Clin. Obstet. Gynec., *2*:705, 1959.
10. Blanc, W. A.: Pathways of fetal and early neonatal infections. J. Pediat., *59*:473, 1961.
11. Bruck, K.: Temperature regulation in the newborn infant. Biol. Neonat., *3*:65, 1961.
12. Buetow, K., and Klein, S.: Effect of maintenance of "normal" skin temperature on survival of infants of low birth weight. Pediatrics, *34*:163, 1964.
13. Chandra, R. K.: Fetal malnutrition and postnatal immunocompetence. Am. J. Dis. Child., *129*:450, 1975.
14. Cocchi, P., Mori, S., and Becattini, A.: Nitroblue-tetrazolium reduction by neutrophils of newborn infants in vitro phagocytosis test. Acta Paed. Scand., *60*:475, 1971.
15. Cockburn, F., Brown, J. K., Belton, U. R., and Forfor, J. O.: Neonatal convulsions associated with primary disturbance of calcium, phosphorus, and magnesium metabolism. Arch. Dis. Child., *48*:99, 1973.
16. Coen, R., Grush, O., and Kauder, E.: Studies of bactericidal activity and metabolism of the leukocyte in full term neonates. J. Pediat., *75*:400, 1969.
17. Cozzi, F., and Wilkinson, A. W.: Low birth weight babies with oesophageal atresia or tracheo-oesophageal fistula. Arch. Dis. Child., *50*:791, 1975.
18. Davies, P. A.: Bacterial infection in the fetus and newborn. Arch. Dis. Child., *46*:1, 1971.
19. Davis, A. T., Blum, P. M., and Quie, P. G.: Studies on opsonic activity for E. coli in premature infants after blood transfusions. Abstr. Soc. Ped. Res., 1971, p. 233.
20. Dery, P., Marks, M. I., and MacKay, E.: Susceptibilities of bacteria to different antibiotic regimens. Am. J. Dis. Child., *129*:328, 1975.
21. Dossett, J. H.: Microbial defenses of the child and man. PED. CLIN. N. AM., *19*:355, 1972.
22. Dossett, J. H., Williams, R. C., and Quie, P. G.: Studies on interaction of bacteria, serum factors and polymorphonuclear leukocytes in mothers and newborns. Pediatrics, *44*:49, 1969.

23. Dubowitz, L., Dubowitz, V., and Goldberg, C.: Clinical assessment of gestational age in the newborn infant. J. Pediat., 77:1, 1970.
24. Fairney, A., Jackson, D., and Clayton, B. E.: Measurements of serum parathyroid hormone, with particular reference to some infants with hypocalcaemia. Arch. Dis. Child., *48*:419, 1973.
25. Fanaroff, A. A., Wald, M., Gruber, H. S., and Klaus, M. H.: Insensible water loss in low birth weight infants. Pediatrics, 50:236, 1972.
26. Fireman, P., Zuchowski, D. A., and Taylor, P. M.: Development of human complement system. J. Immunol., *103*:25, 1969.
27. Fluge, G.: Clinical aspects of neonatal hypoglycemia. Acta Paediat. Scand., 63:826, 1974.
28. Forman, M. L., and Stiehm, E. R.: Impaired opsonic activity but normal phagocytosis in low birth weight infants. N. Eng. J. Med., *281*:926, 1969.
29. Gandy, G., Adamsons, K., Jr., and Cunningham, N.: Thermal environmental and acid-base homeostasis in human infants during the first few hours of life. J. Clin. Invest., *43*:751, 1964.
30. Gitlin, D., and Biasucci, A.: Development of γG, γA, γM, Bic/Bia C'1 esterase inhibitor, Ceruloplasmin, transferrin, hemopexin, haptoglobin, fibrinogen, plasminogen, antitrypsin, orosomucoid, B-lipoprotein, γ_2 macroglobulin, and prealbumin in the human conceptus. J. Clin. Invest., *48*:1433, 1969.
31. Gleiss, J., and Stuttgen, G.: Morphologic and functional development of the skin. *In* Stave, U. (ed.): Physiology of the Perinatal Period, Vol. II. New York, New York, Appleton-Century-Crofts, Inc., 1970, pp. 889–906.
32. Gotoff, S. P., and Behrman, R. E.: Neonatal septicemia. J. Pediat., 76:142, 1970.
33. Gregory, J., and Hey, E.: Blood neutrophil response to bacterial infection in the first month of life. Arch. Dis. Child., *47*:747, 1972.
34. Gruenwald, P.: Chronic fetal distress and placental insufficiency. Biol. Neonat., 5:215, 1963.
35. Hey, E. N., and Katz, G.: The optimum thermal environment for naked babies. Arch. Dis. Child., *45*:328, 1970.
36. Hey, E. N., and Maurice, N.: Effect of humidity on production and loss of heat in the newborn baby. Arch. Dis. Child., *43*:166, 1968.
37. Hey, E. N.. Katz, G., and O'Connell, B.: The total thermal insulation of the newborn baby. J. Physiol. (London), *207*:683, 1970.
38. Hill, J. R.: The oxygen consumption of newborn and adult mammals: Its dependence on the oxygen tension in the inspired air and on environmental temperature. J. Physiol., *149*:346, 1959.
39. Hill, J. R., and Rahimtulla, K.: Heat balance and the metabolic rate of newborn babies in relation to environmental temperature; and the effect of age and of weight on basal metabolic rate. J. Physiol., *180*:239, 1965.
40. Hill, J. R., and Robinson, D. C.: Oxygen consumption in normally grown, small for dates, and large for dates newborn infants. J. Physiol., *199*:685, 1968.
41. Hobbs, J. R., and Davis, J. A.: Serum γG-globulin levels and gestational age in premature babies. Lancet, *1*:757, 1967.
42. Kass, E. H., and Zinner, S. H.: Bacteriuria and pyelonephritis in pregnancy. *In* Obstetric and Perinatal Infections. Philadelphia, Lea and Febiger, 1973, Ch. 21.
43. Klein, J. O.: Current usage of antimicrobial combinations in pediatrics. PED. CLIN. N. AM., *21*:443, 1974.
44. Koeningsberger, M.: Judgment of fetal age. I. Neurologic Evaluation. PED. CLIN. N. AM., *13*:823, 1966.
45. Koivisto, M., Blanco-Sequeiros, M., and Krause, M.: Neonatal symptomatic and asymptomatic hypoglycemia: A follow-up study of 151 children. Develop. Med. Child. Neurol., *14*:603, 1972.
46. Krauss, A. M., and Auld, P. A. M.: Metabolic requirements of low birth weight infants. J. Pediat., 75:952, 1969.
47. Le Dune, M. A.: Intravenous glucose tolerance and plasma insulin studies in small for dates infants. Arch. Dis. Child., *47*:111, 1972.
48. Le Dune, M. A.: Response to glucagon in small for dates hypoglycaemic and nonhypoglycaemic newborn infants. Arch. Dis. Child., *47*:754, 1972.
49. Lubchenco, L. O., and Bard, H.: Incidence of hypoglycemia in newborn infants classified by birth weight and gestational age. Pediat., *47*:831, 1971.
50. Lubchenco, L., Hansman, C., and Dressler, M.: Intrauterine growth as estimated from liveborn birthweight data at 24 to 42 weeks of gestation. Pediatrics, *32*:793, 1963.
51. Mansberger, A. R. N., Boyd, D. R., Crowley, R. A., and Buxton, R. W.: Refractometry and osmometry in clinical surgery. Ann. Surg., *169*:672, 1969.
52. McCracken, G. H., Jr., and Eichenwald, H. F.: Leukocyte function and the development of opsonic and complement activity in the neonate. Am. J. Dis. Child., *121*:120, 1971.
53. McCullough, J., Benson, S. G., et al.: Effect of blood bank storage on leukocyte function. Lancet, 2:1333, 1969.

54. Miller, M. E.: Phagocytosis in the newborn infant: humoral and cellular factors. J. Pediat., 74:255, 1969.
55. Milner, R. D. G.: Neonatal hypoglycemia—A critical reappraisal. Arch. Dis. Child., 47:679, 1972.
56. Mizrahi, A., Lonson, R., and Gribetz, D.: Neonatal hypocalcemia: its causes and treatment. N. Eng. J. Med., 278:1163, 1968.
57. Nachman, R., and Esterly, N.: Increased permeability in preterm infants. Abstract presented at the meeting of the American Pediatric Society and Society for Pediatric Research, Atlantic City, New Jersey, April 28 to May 1, 1971.
58. Pildes, R., Forbes, A. E., O'Connor, S. M., and Cornblatt, M.: The incidence of neonatal hypoglycemia—a completed survey. J. Pediat., 70:76, 1967.
59. Pitt, J.: Passive transfer of milk phagocytes—mechanisms of protection in necrotizing enterocolitis. *In* Necrotizing Enterocolitis in the Newborn Infant. 68th Ross Conference on Pediatric Research, Aug. 1975, p. 53.
60. Plotkin, S. A.: Routes of fetal infection and mechanisms of fetal damage. Am. J. Dis. Child., *129*:444, 1975.
61. Prinbull, G.: Cellular inflammatory reactions in newborns and older infants. Blut, *17*:279, 1968.
62. Roberton, N. R. C., and Smith, M. A.: Early neonatal hypocalcemia. Arch. Dis. Child., 50:604, 1975.
63. Root, A. W., and Harrison, H. E.: Recent advance in calcium metabolism. J. Pediat., *88*:01, 1976.
64. Rowe, M. I., Buckner, D. M., and Newmark, S.: The early diagnosis of gram negative septicemia in the pediatric surgical patient. Ann. Surg., *182*:280, 1975.
65. Rowe, M. I., Lankau, C., and Newmark, S.: Clinical evaluation of methods to monitor colloid oncotic pressure in the surgical treatment of children. Surg. Gynec. Obstet., *139*:889, 1974.
66. Rubner, M.: Ueber den Werth der Weizenkleie füur die Eranähung des Menschen. Z. Biol. Munich, *19*:534, 1883.
67. Saint-Anne Dargassies, S.: The full-term newborn. Neurological Assessment. Biol. Neonat., 4:174, 1962.
68. Saville, P., and Kretchmer, N.: Neonatal tetany; a report of 125 cases and review of the literature. Biol. Neonat., 2:1, 1960.
69. Scopes, J. W., and Ahmed, I.: Minimal rates of oxygen consumption in sick and premature newborn infants. Arch. Dis. Child., *41*:407, 1966.
70. Seth, V., and Chandra, R. K.: Opsonic activity, phagocytosis, and bactericidal capacity of polymorphs in undernutrition. Arch. Dis. Child., 47:282, 1972.
71. Silverman, W. A.: General consideration, relationship between length, weight, surface area and fetal age. *In* Dunham's Premature Infants, 3rd ed. New York, Harper and Row Publishers, Inc., 1964, pp. 56–57.
72. Silverman, W. A., and Agate, F.: Variation in cold resistance among small newborn animals. Biol. Neonat., 6:113, 1964.
73. Sinclair, J. C.: Heat production and thermoregulation in the small for date infant. PED. CLIN. N. AM., *17*:147, 1970.
74. Sinclair, J. C.: Thermal control in premature infants. Ann. Rev. Med., 23:129, 1972.
75. Sinclair, J. C., Scopes, J. W., and Silverman, W. A.: Metabolic reference standards for the neonate. Pediatrics, 39:724, 1967.
76. Stern, L.: *In* Klaus, M. H., and Fanaroff, A. A. (eds.): Care of the High Risk Neonate. Philadelphia, W. B. Saunders Co., 1973, p. 170.
77. Stiehm, E. R.: Fetal defense mechanisms. Am. J. Dis. Child., *129*:438, 1975.
78. Stiehm, E. R., and Fudenberg, H. H.: Serum levels of immune globulins in health and disease; A survey. Pediatrics, 37:715, 1966.
79. Straus, J., Adamsons, K., and James, L. S.: Renal function of normal full-term infants in the first hours of extrauterine life. Am. J. Obstet. Gynec., *91*:286, 1965.
80. Talbot, N. B., Crawford, J. D., and Butler, A. M.: Homeostatic limits to safe parenteral fluid therapy. N. Eng. J. Med., 248:1100, 1953.
81. Talbot, N. B., Crawford, J. D., Kerrigan, G. A., et al.: Application of homeostatic principles to the management of nephritic patients. N. Eng. J. Med., 255:655, 1956.
82. Talbot, N. B., Kerrigan, G. A., Crawford, J. D., et al.: Application of homeostatic principles to the practice of parenteral fluid therapy. N. Eng. J. Med., 252:856, 898, 1955.
83. Tsang, R. C., Light, I. J., Sutherland, J. M., and Kleinman, L. I.: Possible pathogenetic factors in neonatal hypocalcemia of prematurity. J. Pediat., 82:423, 1973.
84. Tsang, R. C., Chen, I. W., Friedman, M. A., and Chen, I.: Neonatal parathyroid function. Role of gestational age and postnatal age. J. Pediat., 83:728, 1973.
85. Uhr, J., Davis, J., and Newmann, C. G.: Delayed type hypersensitivity in premature neonatal humans. Nature, *187*:1130, 1960.
86. Wald, M. K.: Problems in chemical adaptation. *In* Klaus, M. H., and Fanaroff, A. A. (eds.): Care of the High-Risk Neonates. Philadelphia, W. B. Saunders Co., 1973.

87. Walker, W. A.: Immunology of the neonatal gastrointestinal tract. *In* Necrotizing Enterocolitis in the Newborn Infant. 68th Ross Conference on Pediatric Research, Aug. 1975, p. 42.
88. Wallach, E. E., Brody, J. I., and Oski, F. A.: Fetal immunization as a consequence of bacilluria during pregnancy. Obstet. Gynecol., *33*:100, 1969.
89. Widdowson, E.: Growth and composition of the fetus and newborn. *In* Assali, N. (ed.): Biology of Gestation, Vol. II. New York, Academic Press, 1968, p. 33.
90. Winters, R. W.: Maintenance fluid therapy. *In* Winters, R. W. (ed.): The Body Fluids in Pediatrics. Boston, Little, Brown and Co., 1973, p. 119.
91. Wright, W. C., Ank, B. J., Herbert, J., and Stiehm, E. R.: Decreased bactericidal activity of leukocytes of stressed newborn infants. Pediatrics, *56*:579, 1975.
92. Wu, P. Y. K., and Hodgman, J. E.: Insensible water loss in preterm infants: Changes with postnatal development and nonionizing radiant energy. Pediatrics, *54*:704, 1974.
93. Xanthon, M.: Leukocyte blood picture in ill newborn babies. Arch. Dis. Child., *47*:741, 1972.
94. Zweymuller, E., and Preining, O.: The insensible water loss of the newborn infant. Acta Paediat. Scand. (Suppl.), 205, 1970.

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Surgical Aspects of Airway Management in Infants and Children

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The infant or child who has stopped breathing, for whatever cause, requires immediate restoration of respiratory gas exchange. The inexperienced physician may mistakenly attempt to perform emergency oral or nasotracheal intubation as part of the initial resuscitative effort. This is usually a serious mistake. One should not risk the delay and hypoxia associated with an unexpectedly difficult intubation when ventilation and gas exchange can be restored immediately through the use of a bag and mask combination. Even a skilled anesthesiologist can perform a safer intubation if the patient is oxygenated first. The time factor is particularly critical for small infants with pre-existing pulmonary hypertension and the potential for right to left shunt. The delay and associated hypoxemia during a prolonged intubation can reestablish the right to left shunting associated with a fetal circulatory pattern, and this may be irreversible in some small infants. Other problems occasionally coincident with intubation include laryngospasm, cardiac arrhythmias, and trauma to the upper airway. All of these factors emphasize the need for preoxygenation before attempting passage of an endotracheal tube.

The one exception to the immediate use of bag and mask assistance is the infant with a suspected diaphragmatic hernia; in those infants positive pressure applied to the mouth and nose will cause inflation of the herniated stomach and intestine which can cause further compression of the lungs and mediastinum. In such infants, if an increase in the inspired oxygen concentration during spontaneous respiration is not sufficient, respiration must be assisted only following endotracheal intubation.

Proper positioning of the infant during bag and mask assistance is an important factor in the effectiveness of this technique. The "sniff-

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Figure 1. The "sniffing position" with the neck flexed, the head extended on the neck, and the jaw forward.

ing" position, with the neck flexed forward, the head extended on the neck, and the jaw held forward is the most satisfactory position for good gas exchange (Fig. 1).

ENDOTRACHEAL INTUBATION

Any patient requiring respiratory assistance for more than 15 or 20 minutes should be intubated once the initial hypoxemia and hypercarbia have been reversed. Endotracheal intubation permits more efficient and effective control of the upper airway because: (1) there is less gas leak compared with a mask; (2) the airway is isolated from pharyngeal fluids; (3) any upper airway obstruction is bypassed by the tube; (4) the potential for high Valsalva pressures is decreased; and (5) one hand of the person giving assistance can be freed for other functions after the tube is taped securely in place.

Technique

The most useful position for endotracheal intubation, as with bag and mask ventilation, is again the "sniffing" position. This is obtained in the supine patient by elevating the head on a pad to produce a forward flexion of the neck and a hyperextension of the head on the neck. The jaw should be lifted gently but firmly forward. The blade of the laryngoscope should be inserted from the right side of the mouth to allow the flange on the blade to hold the tongue toward the left. The infant larynx is much higher than in adults. It is a common error to insert the blade too deeply, occluding the larynx and exposing the esophageal rather than the tracheal inlet. We prefer a straight blade of appropriate size. In infants it is often helpful to place the blade in the vallecula anterior to

the epiglottis with forward lifting to expose the larynx. The cords and larynx can then be sprayed with 0.2 ml of 4 per cent xylocaine to relieve any laryngospasm present. The endotracheal tube should be passed under direct vision through the cords. The length of the trachea is only 4 centimeters in an infant of average birthweight, and the endotracheal tube must be advanced sufficiently far that movement of the neck will not cause extubation but not so far as to occlude either mainstem bronchus. Centimeter markings on the tube are useful.

Oral Intubation

The oral route is preferred for initial emergency intubation because it is quicker and provides a better "feel" of the tube fit in the airway. It is slightly more difficult to anchor a tube passed through the mouth compared with one passed through the nose. Care must be taken not to tape the tube too tightly against the upper lip because it may cause a pressure erosion of the upper gum (Fig. 2). During passage, the tube should not be forced through the cords or the upper trachea. If the trachea appears to grip the tube tightly, the tube must be replaced for one of smaller size to avoid tracheal mucosal necrosis.

Nasal Intubation

Passage of the endotracheal tube through the nose takes slightly longer, and the procedure may be hampered by unexpected problems such as choanal atresia or an inability to manipulate the tube "around the corner" from the nose into the oropharynx. Preliminary oral tracheal intubation is therefore recommended to evaluate tube fit and to preventilate the patient before an attempt at nasal passage of the tube. A few drops of normal saline can be instilled into the desired nostril as a lubricant before the endotracheal tube is advanced through the nostril to the

Figure 2. Pressure erosion on gum from oral endotracheal tube taped against right upper lip.

Figure 3. Chronic deformity of right ala following long-term nasotracheal intubation.

oropharynx. Bleeding from trauma to the turbinates or adenoids during tube passage may cause significant problems, especially with patients of an age when the adenoids are hypertrophied or if there is a bleeding disorder. The larynx is exposed in the same manner as for oral intubation. Under direct vision, the nasal tube is manipulated to ride anteriorly over the posterior rim of the larynx, sometimes assisted with Magill forceps. The length marking of the tube at the nostril is noted as the tip passes the cords, and the tube is advanced slowly to position the tip between the cricoid and the carina.

The nasal tube should be anchored to the upper lip (not the nose), and further security may be obtained by winding the tape around the back of the head. External bracing of the tube and alternation from nostril to nostril may help to decrease deforming pressure erosion of the ala nasae (Fig. 3). Nasal passage of the endotracheal tube allows a more secure fixation of the tube, minimizes up and down sliding with head motion, and prevents the patient from biting down and occluding the tube. The final position must be checked by chest x-ray, as this is the only way to be certain the tube will not cause obstruction of a bronchus or become dislodged because it barely passes through the glottis. The external length of the tube at the incisor gum line or at the nostril should be noted on the patient's chart once optimum placement has been determined. Occasionally a tube may kink as it makes the bend from the nose to the oropharynx, preventing passage of an adequate suction catheter. This is an indication to reintubate orally.

Tubes

Endotracheal tubes come in a variety of shapes and sizes to meet specific needs (Table 1). Tube sizes are approximate, and occasionally the tube required may be two sizes smaller than the average for the age. For this reason, several sizes must be ready and within reach of the per-

son performing intubation. Long-term placement requires a tube size which allows a slight air-leak to prevent airway trauma. A tight fitting tube might appear to be useful initially, but with time it will cause mucosal necrosis with subsequent scarring and serious stenosis of the upper airway. The smallest diameter of the trachea in an infant is at the subglottic cricoid level. One cannot overemphasize the importance of the loose-fitting tube in order to avoid subglottic stenosis. In children 6 years and over, a cuff may be considered to help maintain a relative seal, but a small leak should still be allowed. This leak can be compensated by larger tidal volumes during ventilation, and a dynamic airway seal may be maintained with a small amount of PEEP (positive end expiratory pressure).

Cuffs are rarely used on infant tubes because of the necessary reduction in tube diameter and the associated major increase in airway resistance associated with the smaller tubes. A satisfactory fit to allow assisted ventilation can be obtained at the cricoid level in infants without the use of a cuff. Tubes for emergency use must be stored in such a way as to retain a lengthwise arc. This fixed arc in the tube facilitates intubation without the encumbrance of a stylet. Occasionally a stylet is needed to bring the tip of the endotracheal tube more anteriorly.

Table 1. *Intubation Equipment*

*Endotracheal Tubes**

AGE	INTERNAL DIAMETER (mm)
Newborn (small)	3.0†
Newborn (large)	3.5
6 to 24 months	4.0
24 to 36 months	4.5
4 years	5.0
5 years	5.5
6 and 7 years	6.0
8 and 9 years	6.5
10 and 11 years	7.0
12 and 13 years	7.5
14 and 15 years	8.0
16 years and beyond‡	8.5

Laryngoscopes

AGE	LARYNGOSCOPE BLADES	ESSENTIAL EXTRAS
Premature and newborn	Miller 0	Stylet
1 month to 1–2 years	Miller 1	Xylocaine Spray 4 per cent
2 years to adult	Miller 2	Suction apparatus
Large adult	Miller 3	Magill forceps, small and large
		Xylocaine 2 per cent with epinephrine

*A loose fit is desirable if the tube is to remain in place more than a few hours, and in this case a smaller tube than listed is ordinarly used. Individual variation as well may require a tube one or even two sizes smaller than suggested.

†A 2.5 Internal Diameter (I.D.) endotracheal tube is rarely necessary.

‡For 2 years of age and beyond, the Internal Diameter (I.D.) usually equals 4.5 mm plus 0.5 mm for each 2 years of age up to 8.5 in females and up to 9.0 or 9.5 I.D. in males.

A forward directed hockey-stick bend at the tube end may be made to solve this problem.

Postextubation Croup

Some degree of mucosal swelling in the trachea and particularly at the subglottic level occurs following even the most gentle introduction of an endotracheal tube. A tight fitting tube or a prolonged intubation is associated with mechanical trauma from manipulation, and machine ventilation is often followed by inspiratory stridor after extubation. We find this complication is most often effectively treated by mask delivered IPPB (intermittent positive pressure breathing) from an inspiration-only nebulizer attached to a ventilator with a pressure responsive cut-off.* This system is used to nebulize and drive the inhalation of 1/4 to 1/2 cc of 0.25 per cent racemic epinephrine (or 1/2 to 1 cc of 0.1 per cent levo epinephrine) with 3.0 or 4.0 cc distilled water. Most treatments are continued until the nebulizer has emptied. The epinephrine has the effect of rapidly shrinking the inflamed mucosa, and the routine is repeated as need requires until significant croup no longer occurs.

MECHANICAL VENTILATION

The indications for mechanical ventilation depend somewhat upon the nature of the patient's underlying condition. Continuous improvements in mechanical equipment as well as monitoring techniques have greatly broadened the applications of assisted ventilation in infant surgical patients.

Monitoring

Frequent determinations of arterial Po_2, Pco_2, and pH are essential for management of patients requiring respiratory support. It is difficult to establish rigid criteria for ventilatory assistance based on blood gas data because values which might be considered indicative of respiratory failure in a patient following an abdominal surgical procedure may on the other hand be considered acceptable in a patient with chronic congenital heart disease. Continuous monitoring is necessary to identify trends and to avert decision by crisis.

Heel stick blood gas values allow a reasonable estimate of the arterial pH and Pco_2, but they may be grossly misleading for arterial Po_2. Umbilical arterial catheters are used frequently for serial blood gas determinations in newborn infants. As with insertion of the endotracheal tube, insertion of the umbilical artery catheter must be followed by x-ray verification of the catheter tip position. Placement of the catheter tip in the lower thoracic aorta can lead to thromboembolic complications in the mesenteric or renal arteries. We recently had one infant expire with infarction of the entire small bowel following dislodgement of a catheter embolus which occluded the superior mesenteric artery. This catheter had been placed in the lower thoracic aorta 4 days previously in an

*Bird Mark VII, Bird Corporation, P.O. Box 2007, Palm Springs, Calif. 92262.

outside hospital. Optimal catheter position is just above the aortic bifurcation and below the inferior mesenteric branch. Radial artery cannulation by the percutaneous method or with direct exposure of the artery in small infants is useful when the umbilical arteries are not available.

After the patient is connected to a ventilator, continuous monitoring is necessary for immediate detection of mechanical problems and ventilator malfunction. We prefer a dual system of monitoring with alarm systems to detect the absence of respiratory circuit pressure and independent alarm systems to detect the lack of ventilation. The latter include noninvasive electret pads, thermistored fluid mats, capacitance plates, or chest impedance detectors. Independence of these monitoring systems from the power source of the ventilator adds an additional margin of safety (Fig. 4).

Frequent examination of the mechanically ventilated patient and his apparatus is essential. Adequate visual monitoring requires the intensive care unit environment with its high nurse-to-patient ratio and personnel trained in the use of special equipment. Various parameters relating to machine function and physiologic monitoring should be kept on a flow sheet for immediate correlation between machine adjustments and patient response.

Ventilators

Infant ventilators have been designed with control mechanisms based primarily on airway pressure, delivery of a fixed gas volume, or a combination of both. Oxygen blenders and PEEP devices are used to achieve desired arterial oxygen tensions, and these are now often standard equipment integral to the ventilator. In many pediatric centers, a minimum of 3.0 cm H_2O of PEEP or, if the ventilator is not pulsing, CPAP (continuous positive airway pressure) is maintained up to the time of extubation. This is intended to compensate for the airway resistance of the small endotracheal tube and to avoid development of large negative intraluminal airway pressures. Current interest has focused upon the system described by Downs et al. as intermittent mandatory ventilation (IMV).[3] IMV allows the patient to breathe at will from the circuit in between machine-driven ventilations. This feature almost

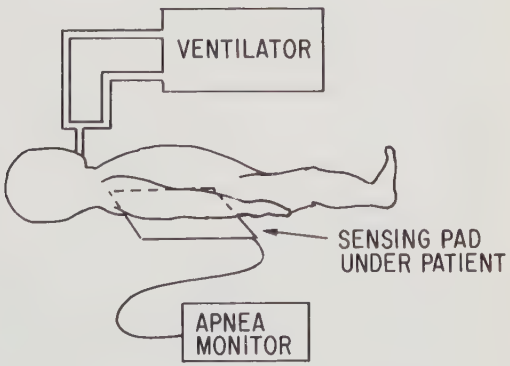

Figure 4. Schematic example of a monitor of respiratory activity separate from the ventilator.

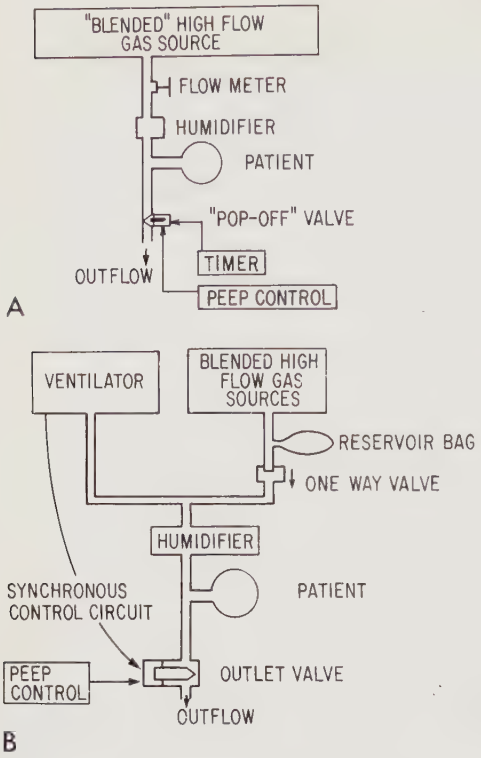

Figure 5. Two types of IMV (intermittent mandatory ventilation) respirator circuits.

eliminates the old phenomenon of "fighting the ventilator" in the lightly sedated patient. The rate of ventilation can be varied smoothly to produce total respiratory control, partial respiratory assistance, or merely increased oxygenation and humidity without any mandatory ventilation. The system also greatly facilitates weaning from the respirator and is extremely flexible for the postoperative management of patients requiring varying periods and degrees of ventilatory support. Proponents also theorize that fewer high peaks in airway pressure per unit time with IMV diminish the chance of pneumothorax. Some IMV devices have been designed to be relatively economical in the use of compressed gas, but most IMV circuits require very high gas flows. IMV is thus considerably easier to use in a facility where compressed air and oxygen are piped in from large storage reservoirs. Hazards may arise where room gas tanks are frequently exhausted by the high flows required. A diagram of two common IMV ventilatory circuits is shown in Figure 5.

TRACHEOSTOMY

Emergency tracheostomy outside of the operating room is rarely if ever indicated in children. In the hospital environment emergency airway control is always more efficiently and safely obtained with bag

and mask followed by endotracheal intubation. Even acute mechanical obstructions secondary to foreign body are more effectively managed by sudden, forced expiration (the Heimlich maneuver) or bag and mask positive pressure ventilation around the obstruction. Tracheostomy may be indicated for congenital or acquired disease of the upper airway or to facilitate long-term mechanical assistance or suctioning because of chronic lung disease. Congenital webs and stenoses, polyps, lymphangiomas, laryngomalacia, papillomas, postinfectious or posttraumatic stenoses, or direct trauma to the larynx are all possible indications for tracheostomy. In every case, however, the tracheostomy should be performed in the operating room under controlled conditions and only after the prior establishment of an airway and adequate ventilation.

The technical procedure of tracheostomy in infants and children varies in several important details from the similar operation in adults. This has been presented in detail previously[1, 8] and only the essential details will be presented here.

Following establishment of a secure airway with an oral endotracheal tube the infant should be positioned on the operating table with the head and neck hyperextended and the shoulders elevated on a towel. A short, transverse skin incision should be made over the trachea at least one finger breadth above the manubrium. If a lower skin incision is made closer to the manubrium the tracheal incision will be deep within the mediastinum. Also, the flange of the tracheostomy tube will ride on the manubrium and cause skin problems and possible tube displacement. The incision need be no longer than 2.0 cm and should be carried in a transverse direction through the platysma. From that point on the dissection is in the vertical midline with separation of the strap muscles by blunt dissection to expose the trachea. It is necessary to incise the pretracheal fascia to expose the tracheal rings. A vertical skin incision is unsatisfactory cosmetically and provides no better or quicker exposure than does the transverse incision. The isthmus of the thyroid is higher in infants than it is in adults, and it is a simple matter to expose the second and third tracheal rings without having to divide or elevate the isthmus. The most important technical feature in the performance of infant tracheostomy is the passage of two silk sutures around the second tracheal ring on either side of the midline for tracheal traction. The upper trachea can be lifted into the incision by means of these sutures, and cumbersome tracheal retractors are unnecessary (Fig. 6). A very small half-circle needle is useful for passing around the tracheal cartilage.

Another important aspect of the procedure is the tracheal incision. A vertical incision should be made through the anterior tracheal midline through two or three cartilages. It is very important that no tracheal cartilage be excised. Excision of a cartilaginous window, as one may do in adults, can produce tracheal wall instability and cause decannulation problems which may prevent removal of the tracheostomy tube. The tracheal incision should be sufficiently long so that the curvature of the tracheostomy tube on its upper aspect does not exert pressure on the upper tracheal ring and cause inward deformity of that tracheal cartilage.

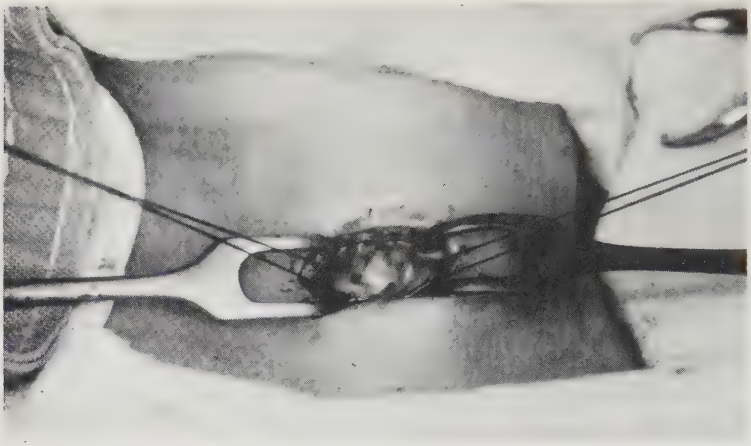

Figure 6. Traction sutures around the second tracheal ring. The endotracheal tube can be seen beneath the vertical incision in the tracheal wall.

Only nonwettable plastic tracheostomy tubes should be used for infants and children. Plastic tubes are flexible and can adapt to the contour of the trachea; they can be cut to proper length in case they are too long. They provide a larger internal diameter for a given external diameter and are less likely to occlude with secretions. The plastic tubes have no inner cannula and require none because they resist occlusion from secretions as long as the inspired air is humidified. Some plastic tubes have no obturator for insertion. This is easily overcome by passing a suction catheter through the tube and into the tracheal incision. With traction on the two tracheal sutures the tracheal opening will gape and the tracheostomy tube can be passed over the suction catheter into the trachea. If the skin incision has been made a proper length, no suturing whatever will be necessary.

The large number of tracheostomy complications reported in small patients emphasizes this is not a minor procedure. Our own experience includes an infant referred following accidental cannulation of the esophagus instead of the trachea. The operating surgeon preoperatively established what he thought was an airway by passing a bronchoscope and then cutting down on the solid object in the neck. The infant was referred following two cardiac arrests and persistent airway obstruction with a tracheostomy tube in the esophagus. Another patient was referred with a stroke following inadvertent cannulation of the carotid artery. A third patient was referred following cardiac arrest and subsequent brain damage secondary to bilateral pneumothorax which occurred during attempted tracheostomy in an emergency room. Pneumothorax during tracheostomy occurs almost always because of struggling against persistent airway obstruction; direct entry of the pleura from the operative site seldom occurs. Additional complications include: iatrogenic tracheoesophageal fistula from incision of the posterior tracheoesophageal septum; erosion of the trachea from a metal tube with or without penetration of the innominate artery; bronchial obstruction

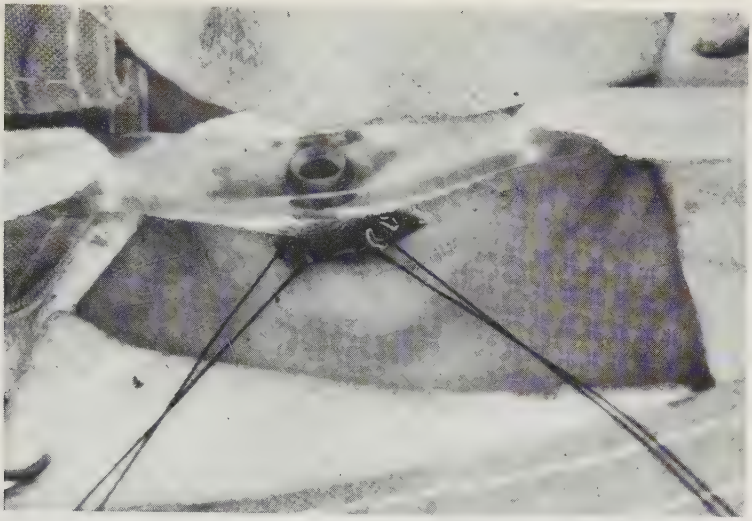

Figure 7. Traction sutures should not be removed for 3 or 4 days following tracheostomy. This facilitates tube replacement in case of accidental decannulation.

secondary to tube irritation; and granuloma formation at the carina. All of these complications can be avoided by adhering to the technical principles outlined above.

Following completing the tracheostomy, the tube should be secured tightly in place with wide tapes. The traction sutures around the second tracheal ring should not be removed but should be taped to the skin of the anterior chest wall (Fig. 7). If the tube should become dislodged within the first 4 days following tracheostomy, it is a simple matter to place traction on the sutures, pull the tracheostomy stoma into the skin incision, and replace the tube. If a tube is not available, the airway can be maintained simply by traction on the sutures to open the tracheostomy incision. After 4 days, the tube tract is fairly well established and the sutures should be removed to prevent any granulation formation on the inner wall of the trachea.

TECHNIQUES FOR TRACHEAL DECANNULATION

Difficulty with decannulation and repeated failure to accomplish removal of the tube in an infant with a tracheostomy is an experience all too familiar in the setting of a large pediatric service.[5] Long and costly hospitalizations have resulted from tracheal extubation failures. If the infant does not remain in the hospital, his care at home with a tracheostomy involves almost constant attention by the parents and a major change in life patterns for the family. It is our experience that virtually all decannulation problems result from mechanical abnormalities of the upper airway which can be corrected. It is rare that an infant cannot be decannulated once the original reason for performing the tracheostomy has passed.

Among the causes of decannulation difficulty are tracheal instability with inspiration, inward deformity of a tracheal ring at the upper margin of the stoma, or an intraluminal granuloma either at the stoma or on the tracheal wall near the tip of the tube. Any or all of these factors can cause airway obstruction following tracheostomy tube removal. The tracheal instability and deformity can and should be prevented by proper technique during the initial tracheostomy. Tracheal instability should not result if cartilage has not been excised and if the tracheal incision has been vertical in the midline. It is also important that the incision be long enough to prevent inward deformity at the upper aspect of the tracheostomy. There is no good way to prevent granuloma formation, but granulomas can and must be excised before attempting decannulation.

Tracheal decannulation requires first that the infant does not have persisting pneumonitis or acute tracheitis and that the secretions are thin and relatively noninfected. The infant should then be tracheoscoped under general anesthesia to evaluate the tracheal lumen. This procedure is necessary to rule out persisting upper airway obstruction from causes such as cord palsy, subglottic stenosis, laryngomalacia, etc. If none of these is present, the most common decannulation problem relates to the presence of granulation tissue which forms at the stoma and around the tracheostomy tube. Removal of the tube while a bronchoscopic telescope is in the upper trachea will reveal whether or not there is obstruction. If obstruction from polypoid granuloma is present anywhere in the airway, it must be removed before decannulation is attempted.

Our own preference for removal of tracheal granulomas is endoscopic resection with an insulated infant urethral resectoscope passed through the larynx. It is usually a simple matter to shave the granuloma from the tracheostomy site with the cutting current. Extreme caution must be used in this procedure. The cutting current must be set low and applied in short bursts to eliminate thermal injury to the surrounding tracheal tissue, and to prevent cutting deeper than intended. A fine suction catheter should be passed next to the resectoscope to evacuate smoke during the resection. We have resected large, polypoid granulomas which almost totally obstructed the tracheal lumen and also granulomas at the carinal level, two of which were partially occluding a mainstem bronchus. Following any such endoscopic resection, it is safest to replace the tracheostomy tube to allow re-epithelialization of the tracheal interior before attempting decannulation.

An alternate method of removing granulation tissue at the tracheostomy site is simple avulsion with a hemostat, but this should be monitored by direct inspection through a bronchoscope to make sure all tissue is removed cleanly. If this procedure is not effective, another more precise method involves excision of the tracheostomy stoma with careful dissection inside the cartilaginous edge of the tracheal incision to slide the mucosa with the granuloma outward into the wound where it is amputated (Fig. 8). If granuloma is removed in this fashion we recommend direct closure of the tracheostomy stoma. This produces stability of the anterior tracheal wall, more rapid healing of the underlying

mucosa, and allows a more effective intratracheal pressure for postoperative cough. If there is inward deformity of the cartilaginous ring at the upper aspect of the tracheostomy stoma this must be corrected by a plastic revision of the anterior tracheal wall before decannulation is attempted.

Once we have ascertained there is no mechanical obstruction to the upper airway, the infant is sedated in the intensive care unit and the tracheostomy tube is merely slipped out. With small infants using the smallest size tracheostomy tube there is no point in attempting progressive decrease in size of the tube since smaller tubes do not exist. We find that fenestration with plugging of such tubes offers no advantage and actually is more risky in terms of occlusion by secretions than actual removal of the tube. Removal is safe providing one has determined beforehand that there is no mechanical airway obstruction, that the anterior tracheal wall is stable, and that decannulation takes place in an intensive care unit where the infant can be observed continuously. Sedation is helpful to decrease the occasional panic that occurs once airway resistance has been changed by decannulation.

Once the tracheostomy stoma has contracted and mostly closed we feel it essential to repeat tracheoscopy in infants for final evaluation of the upper airway. On three occasions we have achieved successful decannulation only to see subsequent tracheal obstruction develop 6 to 10 days later. The tracheostomy closes both by wound contraction and by granulation tissue formation. Occasionally this granulation tissue will expand into the trachea following decannulation and cause a late obstruction.

Sometimes an infant may tolerate initial decannulation only to develop problems from secretions and pulmonary infection 3 or 4 days

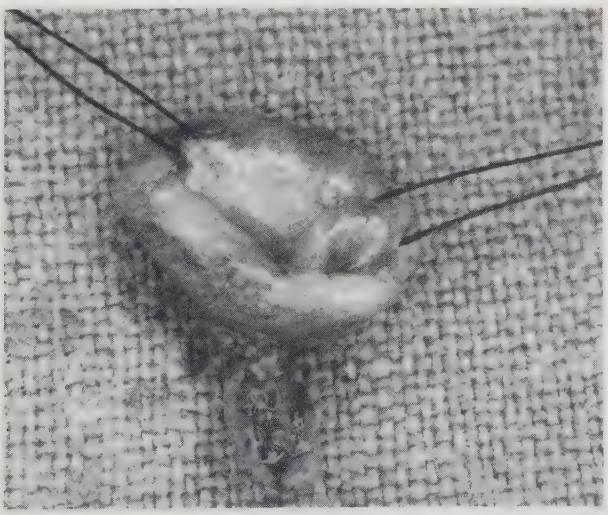

Figure 8. Excised skin and mucosa of tracheostomy stoma with intraluminal tongue of polypoid granuloma. This caused obstruction 10 days following removal of a tracheostomy tube.

later. On four occasions we have successfully excised the tracheostomy site, performed a plastic closure of the trachea, and intensified efforts with pulmonary physiotherapy. Surgical closure of the tracheostomy stoma has apparently improved the infant's efficiency in raising his own secretions and allowed us to carry through with decannulation successfully. This technique is not recommended for routine decannulation because it is not usually necessary. It has proven useful on a few occasions, however, when decannulation appeared otherwise impossible.

POSTINTUBATION SUBGLOTTIC TRACHEAL STENOSIS

Acquired tracheal subglottic stenosis is being seen with increasing frequency in small infants as a byproduct of more advanced methods of respiratory support. Small premature infants in the 1000 gm range who previously would not have survived serious respiratory problems in the newborn period are being managed satisfactorily with more sophisticated techniques. Most of these infants require endotracheal intubation for variable periods of time. An unfortunate byproduct of the intubation has been the increasing frequency of tracheal subglottic stenosis. This scarring in the region of the cricoid is not necessarily related only to length of time the tube is indwelling in the trachea. It seems probable it is related to factors such as tightness of tube fit, the amount of motion and secondary trauma associated with attachment to a ventilator, and the degree of associated infection in the trachea. We have seen postintubation subglottic stenosis of serious degree develop after intubation as brief as 1 day. We have also seen infants successfully extubated following 2 months of endotracheal intubation. The small infant with stiff lungs appears to be at greatest risk from this complication. The small tracheal size limits the range of tube size available and increases the possibility that the tube fit may be too tight and cause secondary mucosal necrosis. In addition, the decreased pulmonary compliance leads to the tendency toward using a larger tube to lessen airway resistance and to decrease the air leak and improve lung inflation. Finally, when the infant with the small trachea is extubated, even a small degree of swelling or scarring in the cricoid region has a relatively large effect upon airway resistance and increases the possibility tracheostomy will be required.

The common first manifestation of tracheal subglottic stenosis is the inability to remove an endotracheal tube because of airway obstruction. This usually leads to tracheostomy. The duration of time the tracheostomy tube is required depends upon the degree of subglottic scarring and the therapeutic approach toward correcting it. We have followed three infants with subglottic stenosis who were extubated successfully following long-term ventilator support for infantile respiratory distress syndrome. These same infants were hospitalized 3 to 6 months later with severe upper respiratory obstruction precipitated by an acute respiratory infection. When the upper airway obstruction did not respond to the usual therapeutic methods for infectious croup, the infants were tracheoscoped and a severe degree of subglottic stenosis was iden-

tified (Fig. 9). In one infant, a web of scar had grown right across the subglottic tracheal lumen leaving openings of only 1 mm above and below this band to allow gas exchange.

The surgical management of subglottic stenosis in infants is challenging. The techniques of sleeve resection of the trachea with end-to-end anastomosis which have been used for tracheal stenosis in adults are not applicable for subglottic stenosis in infants. In the adult situation, acquired postintubation tracheal stenosis is usually secondary to a balloon cuff around an endotracheal tube. The cuff lies at a lower level in the trachea, and the resultant stenotic ring can be excised with anastomosis of the trachea below the laryngeal mechanism. In the infant the tracheal trauma associated with endotracheal intubation occurs at the narrowest diameter in the trachea which is at the cricoid level. It is not possible to resect the cricoid and perform reanastomosis without risking irreparable damage to the laryngeal mechanism. The traditional approach to management has been one of tracheostomy plus a waiting period of several years in the hope growth of the trachea would compensate for the stenosis in the upper airway. With milder forms of subglottic stenosis this is effective, and this may still be the preferable approach for some cases. The inconvenience and morbidity associated with long-term tracheostomy care, however, have led to a search for more direct solutions to the problem of subglottic stenosis. Treatment by multiple tracheal dilatations with a tracheostomy tube in place has been tried and recommended by many authorities, but the results have been disappointing in general. Fearon and Ellis[4] reported that 18 of 23 cases treated with dilatations required tracheostomy care from 1 to 3 years, while five cases still had a tracheostomy in place beyond 3 years. More recently, tracheal dilatation has been combined with direct injection of corticosteroids into the subglottic scar. The steroid injections appear to decrease the necessary number of dilatations, but reported cases have required from six to twenty dilatations over a 120 to 180 day inter-

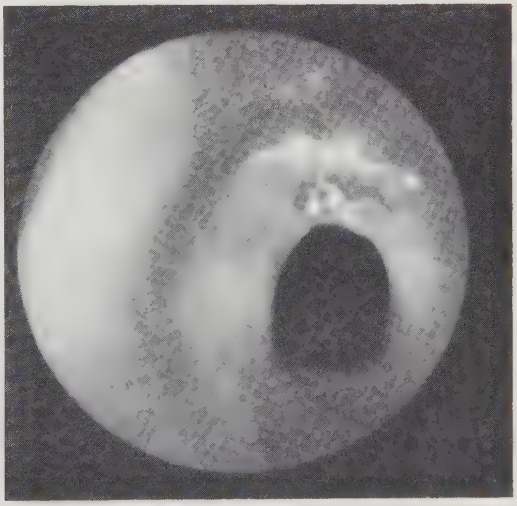

Figure 9. Diaphragm-like postintubation subglottic scar at cricoid level below vocal cords.

val.[9] In 1970, Birck described a method for treating subglottic stenosis using a molded intraluminal plastic stent combined with dilatations and the systemic administration of corticosteroids.[2] Otherson subsequently combined Birck's method of the intraluminal stent with the direct injection of corticosteroids into the subglottic scar.[7]

Our own experience involves the use of all of the above methods plus a newer approach with endoscopic resection of the subglottic scar. This is most often performed with a protecting tracheostomy in place, but on three occasions we have successfully resected a subglottic stenosis endoscopically without the requirement for a protecting tracheostomy. Our experiences are reported in detail elsewhere.[6] The technical aspects of this procedure, however, are very exacting, and the description of the technique is therefore quoted in full from our previous paper:*

TECHNIQUE

Control of the infant's airway is an absolute necessity prior to any attempt at endoscopic resection of subglottic scar. If a tracheostomy has not been performed prior to evaluation of the subglottic stenosis, this evaluation must be performed cautiously with a ventilating bronchoscope. The magnified view through the zero degree infant bronchoscopic telescope is essential. If the smallest 2.5 sheath (4.0 mm O.D. at flare) will not pass through the stenosis at the cricoid level, we believe a tracheostomy should be performed before proceeding with further manipulation. If the 3.0 sheath (5.2 mm O.D.) will pass with minimal resistance but the 3.5 (6.5 mm O.D.) will not, the thickness of the stenotic ring should be evaluated before making a decision regarding tracheostomy. Thin webs and those which are predominantly in the anterior one-half circumference of the trachea may be resected without requiring temporary supplemental tracheostomy. The thicker scars and those which are circumferential are more difficult to manage. If amenable to endoscopic resection, the complicated scars are more safely managed with a staged approach involving quadrant excisions and a protecting tracheostomy. We have allowed an interval of 2 to 4 weeks between stages to permit re-epithelialization over the previously excised quadrant.

The instrument we have found most useful for this procedure is the infant urethral resectoscope with a size 13 insulated sheath (3.5 × 5.0 mm O.D.) and the zero degree rod lens telescope with fiber optic illumination.† Adequate ventilation can be maintained in an infant as a semiclosed system by attaching the anesthesia circuit to the irrigating channel of the resectoscope sheath.

The resectoscope is introduced into the larynx and through the cords by using a laryngoscope for exposure. Thereafter the instrument is advanced to or beyond the cricoid level of the trachea by direct vision through the telescope. Prior introduction of a fine suction catheter to lie beside the resectoscope sheath in the trachea is useful to evacuate any vapor which may arise when the cutting loop passes through the subglottic scar. If the airway is not protected by a tracheostomy the resection should not be initiated until it has been determined that ventilation is adequate and under complete control. The resectoscope sheath is then withdrawn to a level just proximal to the subglottic ring and distal to the vocal cords. The cutting loop is extended behind the web of scar as a hook and the cutting current is then applied. One should start with a very low current and increase until effective cutting is obtained without the bursting effect from excess

*Johnson, D. G., and Stewart, D. R.: Management of acquired tracheal obstructions in infancy. J. Pediat. Surg., *10*:709–717, 1975.

†Manufactured by K. Storz, Storz Endoscopy-America, Inc., 650 South San Vicente Blvd., Los Angeles, Calif. 90048.

heat which will damage surrounding tissue. Very short pulses of current produced by quick taps on the foot pedal will provide precise control during the excision.

A one-half circumference thin web can be excised entirely. Thicker circumferential scars should be attacked in three or four stages. We avoid any excision in the posterior midline to eliminate the danger of esophageal perforation. Following the resection a mixture of triamcinolone (40 mg per ml) with hyaluronidase (150 μg per ml), mixed 5.0 ml per 1.0 ml, can be injected in 0.1 ml volumes into the four quadrants of the subglottic lesion. If ballooning of the muscosa follows the injection, an endotracheal tube is left in place for 1 to 2 hours and then the infant is extubated in the intensive care unit. We have also administered systemic dexamethasone (2.0 mg per 5.0 kg) at the time of resection and 12 hours later without any evidence for or against its effectiveness in limiting postoperative swelling.

SUMMARY

The surgical management of the upper airway in infants and children varies in many important details from the principles of airway management usually applied to adults. Recent technical adaptations and innovations have improved our ability to deal with upper airway obstruction effectively. Advances in respiratory support for sick infants have saved thousands of lives and at the same time produced a new spectrum of airway problems which must be dealt with effectively. The surgeon who takes on such problems should be specially trained and dedicated to the unique requirements of infants and children.

REFERENCES

1. Aberdeen, E.: Tracheostomy and tracheostomy care in infants. Proc. Roy. Med., *58*:900–902, 1965.
2. Birck, H. G.: Endoscopic repair of laryngeal stenosis. Tr. Am. Acad. Ophth. Otol., *74*:140–143, 1970.
3. Downs, J. B., Perkins, H. M., and Modell, J. H.: Intermittent mandatory ventilation: An evaluation. Arch. Surg., *109*:519–23, 1974.
4. Fearon, B., and Ellis, D.: The management of long term airway problems in infants and children. Am. Otol., *80*:669–677, 1971.
5. Greenberg, L. M., Davenport, H. T., et al.: Method for difficult decannulations in children. Arch. Otolaryng., *81*:72, 1965.
6. Johnson, D. G., and Stewart, D. R.: Management of acquired tracheal obstructions in infancy. J. Pediat. Surg., *10*:709–717, 1975.
7. Otherson, H. B., Jr.: The technique of intraluminal stenting and steroid administration in the treatment of tracheal stenosis in children. J. Pediat. Surg., *9*:683–690, 1974.
8. Stool, S. E., Campbell, J. R., and Johnson, D. G.: Tracheostomy in children: The use of plastic tubes. J. Pediat. Surg., *3*:402–407, 1968.
9. Waggoner, L. G., Belenky, W. M., and Clark, C. E.: Treatment of acquired subglottic stenosis. Am. Otol., *82*:822–826, 1973.

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Neonatal Necrotizing Enterocolitis: An Update on Etiology, Diagnosis, and Treatment

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Necrotizing enterocolitis (NNE) is a unique surgical disease of the neonate characterized by diffuse or patchy intestinal necrosis, accompanied by sepsis, and often followed by perforation, peritonitis, and death. The term "unique" is used to indicate that this condition, in contrast to most other neonatal surgical emergencies, is acquired and not congenital, and can be successfully treated without operation in most cases.

In this review we will consider the predisposing factors, criteria for clinical diagnosis, appropriate medical and operative treatment, and give current thoughts on etiology and prevention.

INCIDENCE

The numbers of babies born with congenital malformations has decreased remarkably during the past decade since the advent of birth control measures, the availability of abortion, and genetic counseling. Coincident with the decreased birth rate is an increasing emphasis on intensive neonatal care, particularly in resuscitation of the premature and high risk newborn. NNE is a condition occurring with increasing incidence, proportionate to the neonatologist's success in improving the survival rate of these patients. It has become the single most common surgical emergency in our Newborn Special Care Unit. In the past 6 years, the birth rate in Connecticut has decreased by almost 30 per cent but the incidence of NNE among our operated patients during this period has risen from an average of 3 to 15 per cent (Fig. 1). This, of course, does not take into consideration the large number of others medically treated who survived without operation.

The increased incidence of NNE is a national phenomenon, occurring in 3 to 8 per cent of all premature infants in intensive care centers.

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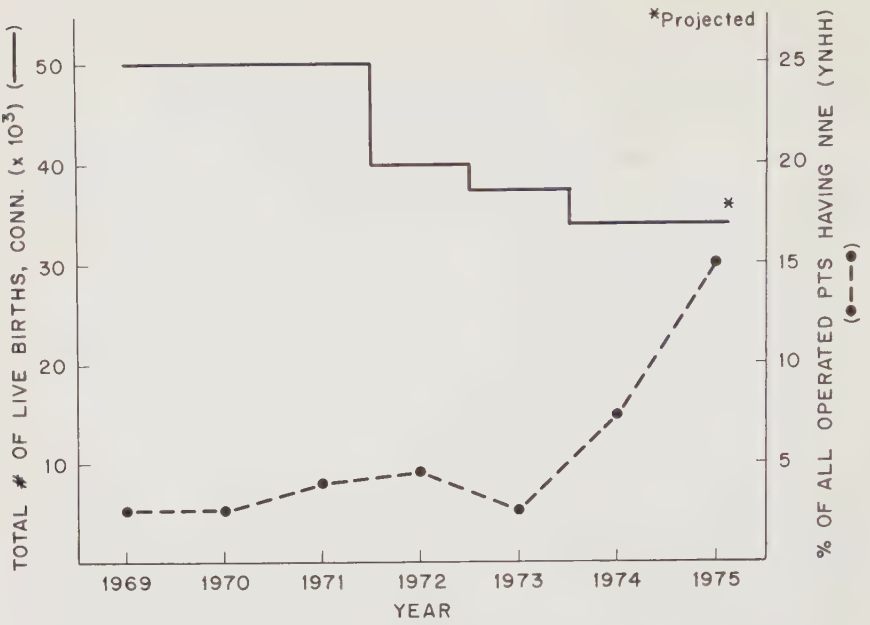

Figure 1. Increasing incidence of NNE amongst operated patients admitted to the Newborn Special Care Unit of the Yale-New Haven Hospital between 1968 and 1975.

The incidence of cases of enterocolitis was just over 6 per cent of the total number of neonates admitted with intestinal obstruction at the Queen Elizabeth Hospital for Children in London.[7] Large series have been reported also from France,[30] Costa Rica,[27] Hungary,[6] and Singapore.[34]

DIAGNOSIS

The infant at risk for developing NNE is a premature newborn weighing 1500 gm or less who has sustained significant perinatal stress. Prenatal complications reported include premature rupture of the membranes, placenta previa, maternal sepsis, and toxemia of pregnancy. Breech delivery and C-section occur in 15 to 20 percent of cases,[31] both proportions being higher than normal.

More common, however, is a specific postpartum respiratory or cardiovascular complication including apnea, respiratory distress syndrome, cyanotic congenital heart disease, hypothermia, or erythroblastosis fetalis. Apgar scores tend to range between four and six which is appropriate for a baby premature by dates and rules against any major intrauterine catastrophe. The relative incidence of these complications in previous reports is summarized in Table 1.[9, 31, 32, 36, 45, 46]

These babies are almost uniformly premature, acidotic, hypoxic and hypothermic, and are usually referred to a regional neonatal intensive care unit where resuscitation includes routine placement of umbilical

Table 1. *Pre- and Postnatal Conditions Associated with NNE*

	INCIDENCE (PER CENT)
PRENATAL	
Premature birth (<2000 gm)	68 to 80
Premature rupture of membranes	25 to 35
Placenta previa	15 to 30
Puerperal sepsis	8 to 10
Toxemia of pregnancy	8
POSTNATAL	
Apneic spells	13 to 50
Respiratory distress syndrome	50 to 60
Temperature instability	35 to 87
Prior sepsis	30 to 43
Cyanotic congenital heart disease	10 to 15
Patent ductus arteriosus	10 to 30
Umbilical artery catheterization	25 to 60
Exchange transfusion	15 to 45

venous and arterial catheters for monitoring blood gases and administering fluids. Umbilical venous exchange transfusion is necessary in certain, albeit diminishing, numbers of infants with Rh incompatibility. When given, feedings have been administered through a gavage tube. Recent interest in high volume gavage, hyperosmolar feedings, and nasojejunal feedings in the premature infant are of significance in defining further the at-risk population.

The appearance of gastrointestinal signs occurs between the first 24 hours of life and the 10th day in over 90 per cent of cases. The initial finding is soft abdominal distention with retention of gastric secretions. These secretions are usually clear but then become bile-tinged. Meconium has been evacuated normally in most, in distinction to Hirschsprung's disease where delayed evacuation occurs in over 90 per cent of cases. Bloody or mucoid diarrhea, while considered a hallmark for primary infectious forms of enterocolitis, is seen in only about 25 per cent of babies with NNE. When gross bleeding occurs early it is often streaked on the surface of meconium and later has a more watery consistency. Occult blood loss does occur in a significantly larger number; it should be checked by guaiac or Benzidine testing. Santulli,[31] Dudgeon,[9] and Wayne and Burrington[45] have directed attention to the importance of localized erythema and induration of the abdominal wall overlying necrotic, possibly perforated, intestine. The subsequent course can vary, but the untreated, sick baby deteriorates rapidly, showing signs of sepsis. This is manifested primarily by thermal instability, lethargy, metabolic acidosis, jaundice, disseminated intravascular clotting (DIC), and then death.

Thrombocytopenia occurs commonly in babies with necrotizing enterocolitis; mean platelet counts range between 50,000 and 75,000 per cubic mm until clinical recovery. The infant with NNE does not commonly have DIC even though the platelet count may be low enough to

cause clinical bleeding. Petechiae and oropharyngeal bleeding were the first manifestations of DIC in Wilson and Woolley's series.[45] Clinical evidence of DIC is usually accompanied by further deterioration; it cannot be reversed until the necrotic intestine is resected. The general impression that DIC occurs in patients with necrotic intestine suggests that tissue thromboplastin released from the damaged bowel is responsible for this complication of NNE. Hematologic testing is important because the appearance of DIC is a guide to determining the course of treatment. Frantz et al.[12] make the laboratory diagnosis of DIC on the basis of decreasing platelet concentration, increasing prothrombin and partial thromboplastin times, and a serum factor V concentration of less than 40 per cent.

The frequency of positive blood cultures ranges from 20 to 70 per cent.[9, 31, 32, 36 37, 45.] The majority of cases culture Escherichia coli, Klebsiella, Enterobacter, and Proteus. Positive cultures for anaerobic gram-negative organisms are rarely seen, despite their early appearance in the gastrointestinal tract of the neonate. Peritoneal fluid cultures taken at the time of operation have the same distribution of gram-negative organisms except for the higher incidence of anaerobes, particularly Bacteroides, which is almost always accompanied by at least one other bacterium. The episodic nature of NNE reported in some nurseries has raised the possibility of a transmissible cause. Virnig and Reynolds[44] investigated a sudden outbreak during a 1-month period but no bacteria, virus, or fungus could be isolated common to the infants involved. This supports the belief that the organisms involved in NNE are normal bowel flora.

The key to making an early diagnosis is to suspect the possibility of NNE in a baby with suggestive clinical signs and to look for confirmatory roentgen findings. The earliest sign is nonspecific intestinal dilatation, which has the appearance of a functional or adynamic ileus without mechanical obstruction. Some degree of intestinal distention is found in almost every patient. A correct interpretation of these films is important in distinguishing NNE from meconium ileus, intestinal stenosis, meconium plug syndrome, and Hirschsprung's disease. Pneumatosis or intramural air is a pathognomonic sign of NNE, particularly in the clinical setting described; it is found in 70 to 80 per cent of reported cases of documented NNE. Unfortunately, pneumatosis is easily overlooked since it may be very localized and can resemble normal fecal matter. Pneumatosis is observed either as a linear stripe alongside a gas-filled intestinal loop or as bubbles of gas in a similar location. These collections occur anywhere from stomach to rectum but are most often seen on the right side of the abdomen in the area of the ileum and ascending colon and within the rectosigmoid as observed on lateral films of the pelvis.

Portal vein gas occurs in about one quarter of babies with NNE, and is most easily detected by its arborizing pattern over the opaque liver shadow as seen on the left lateral view of the abdomen. This is a foreboding sign usually seen in the sickest infants; they are often septic and jaundiced. While previously thought to be a terminal finding, infants

with portal vein gas have survived following aggressive medical treatment.

A pneumoperitoneum is the least common but most important roentgenographic sign and indicates that the intestine is perforated. It may be the initial finding in some patients with localized disease or a later finding in the preterminal infant with extensive necrosis of the intestine. A pneumoperitoneum is difficult to detect on a supine film although it may be observed by defining the umbilical ligament as a linear shadow surrounded by a less dense shadow, the so-called "football sign." Free air under the diaphragm on an upright and lateral view is a much more predictable and safer way to recognize a small pneumoperitoneum.

The use of continuous positive airway pressure techniques in babies with the respiratory distress syndrome has resulted in a remarkable increase in the incidence of pneumomediastinum and pneumothorax. Lee and Kuhn[21] reported a case of pneumatosis intestinalis without NNE following pneumomediastinum in a newborn infant while Leonidas et al.[23] showed that a pnemoperitoneum can also occur under these circumstances. Donahoe et al.[8] demonstrated in experimental studies on rats that air dissects from the mediastinum into the retroperitoneal tissues through the diaphragmatic foramina and descends between the leaves of the mesentery before finally rupturing into the free peritoneal space. The clue to the benign nature of free intraperitoneal air in these cases is the nearly simultaneous radiographic appearance of pneumomediastinum or a pneumothorax.

Occasionally the question of Hirschsprung's disease is raised in the differential diagnosis, particularly when the baby is full-term, a situation which occurs about 20 per cent of the time. Diagnostic barium enema performed in the sick infant with acute necrotizing enterocolitis does, however, carry significant risk of colon perforation and may be confusing because of a "pseudotransitional zone." Burrington[45] reported that three of five patients having a barium enema perforate. Three of nine patients in Santulli's[31] group showed delayed evacuation of the barium for over 24 hours, and a "pseudotransition" mimicking aganglionic megacolon was observed in one other patient.[37] Thus, barium enema can be misleading or even dangerous in babies who probably have acute NNE.

MEDICAL MANAGEMENT

Prompt recognition and treatment are essential for survival. The progressive features of NNE can be aborted if nasogastric suction, intravenous fluids, and systemic antibiotics are begun before the baby develops overt signs of sepsis. In our nursery, any susceptible baby who has gastric retention accompanied by radiographic signs of distention is immediately cultured (blood, throat, stool) and begun on the regimen outlined. Our choice of antibiotics is ampicillin (150 mg per kg per 24 hr) and kanamycin (15 mg per kg per 24 hr). Gentamycin (3 to 5 mg per

kg per 24 hr) may be more effective against E. coli, Klebsiella, and Enterobacter in nurseries with a significant percentage of kanamycin-resistant coliform organisms.

A report from Cincinnati[2] indicates that perforation can be prevented by instillation of topical antibiotics (kanamycin and gentamycin) in twice the usual parenteral dose through the nasogastric tube. This tube is clamped for 1 hour after each dose and the regimen continued until 48 hours after resolution of radiographic and clinical findings. Thirteen consecutive critically ill infants with pneumatosis intestinalis were treated without a single episode of perforation. This therapy is subject to the criticism that the study did not include bacteriology of the stool to demonstrate a quantitative reduction in organisms. Although the ultimate role of topical antibiotics is not fully determined, its use can be encouraged since there are no known detrimental effects.

Low molecular weight dextran has proven effective. In the initial report by Krasna et al.,[20] dextran 40 in the form of a 10 per cent solution was administered intravenously in doses of 10 ml per kg every 6 hours for 48 hours. Four of eight babies receiving the dextran treatment did not require operation while all of the patients not receiving dextran did. In addition, the dextran treated group was protected from later complications, including stricture formation. The mechanism for this apparent protective effect of dextran is due to a combination of factors, including a reduction of platelet adhesiveness and aggregation; by decreasing blood viscosity, perfusion of the gut is also improved.

One of the most important considerations of medical therapy is continued nutritional support with peripheral parenteral alimentation. It is possible to maintain nearly adequate caloric intake using a 12.5 per cent solution (10 per cent glucose, 2.5 per cent protein hydrolysate) for several days. We prefer this route to total parenteral nutrition because of the risk of catheter sepsis in a baby with a bacteremia. Of obvious importance is correction of metabolic acidosis and electrolyte imbalance. Umbilical venous or arterial catheters should be removed at the first signs of NNE and blood gas monitoring continued from a temporal or radial artery. Monitoring of blood pressure by the Doppler technique is a valuable guide to intravascular volume, and together with urine flow, specific gravity and general physical appearance is helpful in determining fluid replacement with plasma or whole blood.

INDICATIONS FOR OPERATION

Essential to successful management is frequent, careful reexamination of the abdomen and serial abdominal films, usually at 6-hour intervals. The emphasis is placed on detecting the earliest possible evidence for perforation or full-thickness intestinal necrosis with pending perforation (Fig. 2). Improved survival depends upon an aggressive approach, including operation on even the smallest babies at the first clear cut sign of peritonitis.

The recognized physical signs of peritonitis include: (1) persistent

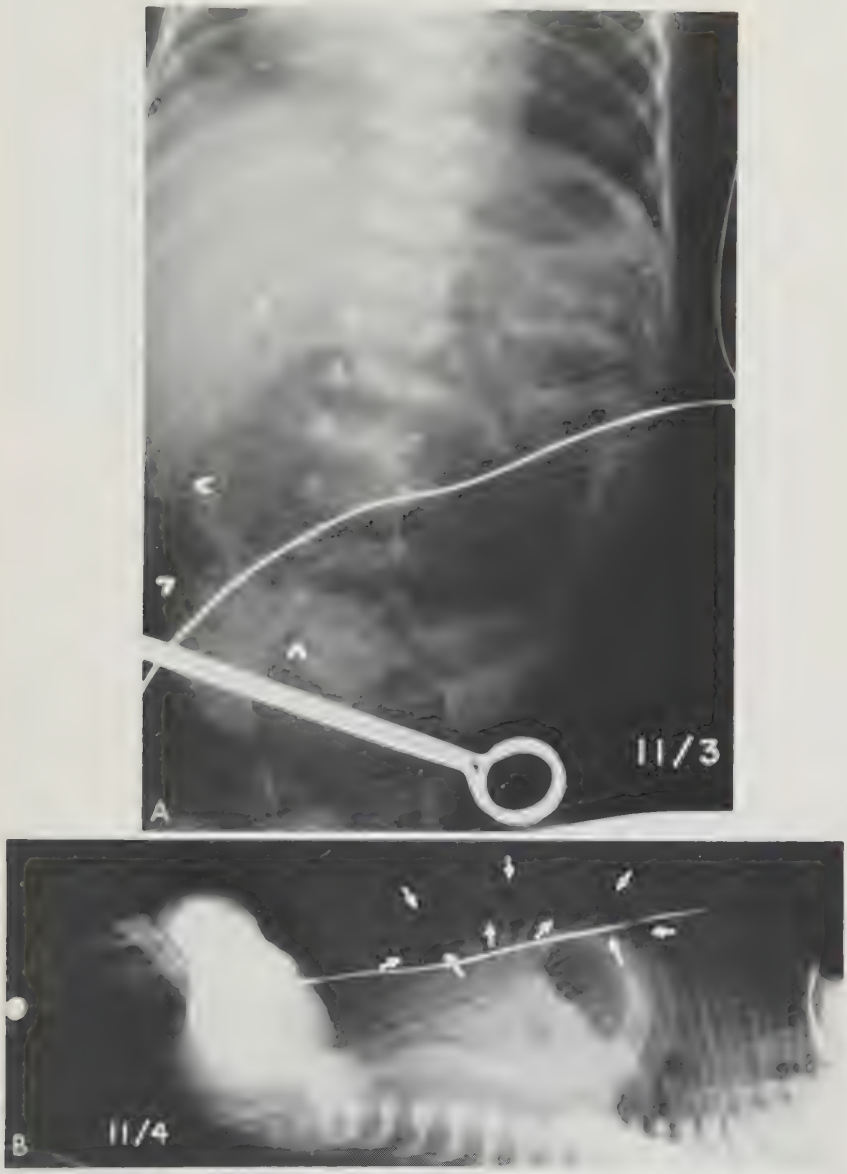

Figure 2. *A*, 1100 gm male with pneumatosis, progressing within 24 hours to perforation of the ileum. *B*, Pneumoperitoneum is visible over the liver shadow on a "cross-table" lateral film.

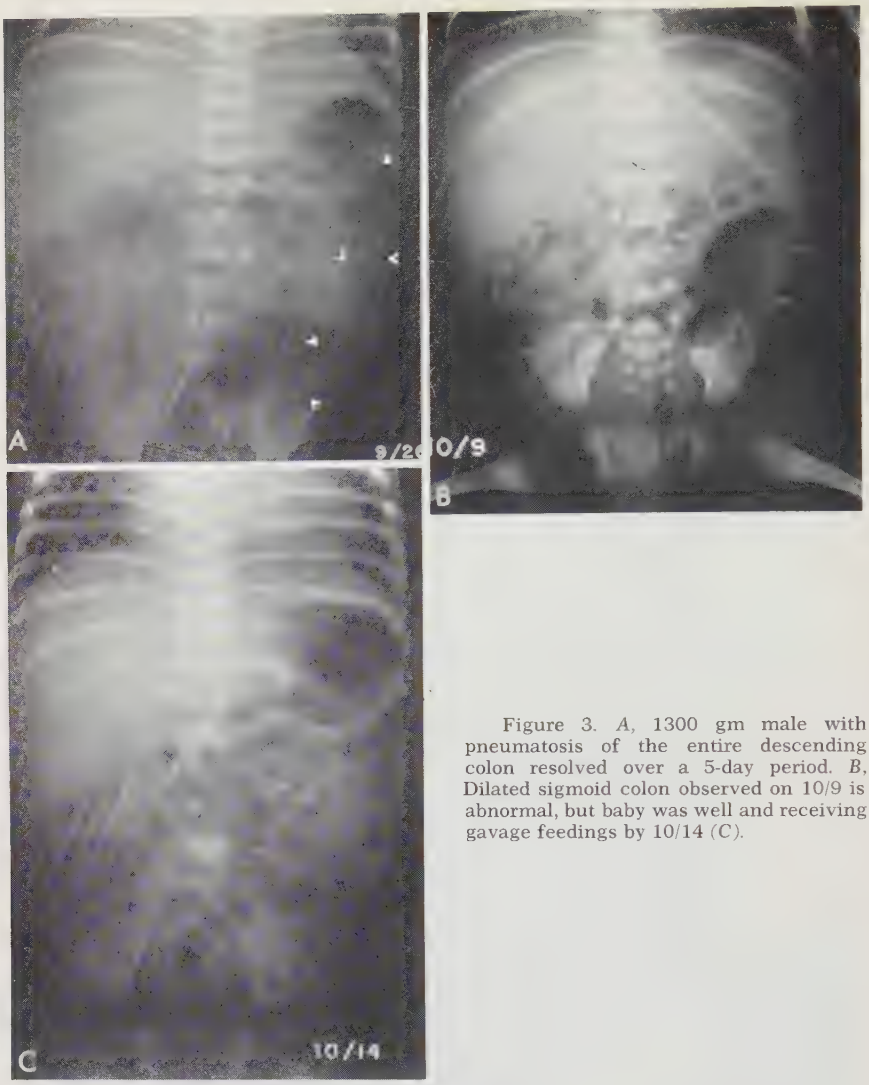

Figure 3. *A*, 1300 gm male with pneumatosis of the entire descending colon resolved over a 5-day period. *B*, Dilated sigmoid colon observed on 10/9 is abnormal, but baby was well and receiving gavage feedings by 10/14 (C).

or well localized signs of abdominal resistance; (2) induration, edema, or cellulitis of abdominal wall; (3) an abdominal mass. Continued nonoperative treatment of infants with these findings is almost uniformly unsuccessful. A single dissenting opinion is offered by Reid and Shannon[29] who reported 10 cases of NNE with appropriate clinical and radiographic criteria for operation; pneumatosis was present in all, pneumoperitoneum in four, and six had radiologic and clinical evidence of abscess formation in the right lower quadrant. With aggressive medical management, nine of the ten patients survived; four eventually had resection of a stricture in the terminal ileum. This purely medical approach to complicated acute NNE and its excellent results have not been duplicated by others.

A pneumoperitoneum has traditionally been the sine qua non radiographic criterion for operation. This continues to be the prime indication except when a benign pneumoperitoneum in a baby with RDS is suspected. In Burrington's experience,[45] the presence of a persistently dilated intestinal loop, usually with associated pneumatosis, is an additional radiographic indication for operation. It is important to reemphasize, however, that pneumatosis alone has proven to be a totally reversible finding in about 50 per cent of babies receiving vigorous and early medical treatment (Fig. 3).

Four of 14 patients in Leonidas' series[22] had radiographic signs of ascites, including bulging of the flanks, diffuse haziness of the abdomen, separation of intestinal loops, and a centralized position of the bowel. These findings were accompanied by clinical deterioration. The diagnosis of peritonitis was confirmed at operation and in two infants an intestinal perforation was found which was undetected clinically or radiographically before surgery. Therefore, the presence of increasing intraperitoneal fluid should also be considered a radiographic indication for operation.

Signs of intestinal obstruction can occur during the acute or early stages of NNE from inflammatory changes and angulation of the intestinal wall or from a walled-off perforation with abscess formation. Three of 64 patients in Santulli's group[31] had obstruction without pneumatosis and the diagnosis of necrotizing enterocolitis was made at operation. More important, however, is the increasingly larger number of babies reported with late intestinal obstruction from intestinal strictures following resolution of sepsis and resumption of feedings (Fig. 4). Originally described to occur in the colon,[19] the ileum and even jejunum may also obstruct. In the past year alone we have treated three patients with intestinal strictures compared to only one in the previous 5-year period. This attests to the effectiveness of the early institution of medical treatment which prevents perforation and promotes healing, albeit with scar formation. The period of delay between resumption of feedings and the onset of obstruction varies from 4 weeks to as long as 3 months. Other complications that we have seen are chronic anemia from a large ulcer proximal to a stricture in the jejunum and sigmoidocutaneous fistula at the umbilicus (Fig. 5).

OPERATIVE TREATMENT

There should be no delay in operation for a deteriorating baby with appropriate clinical and radiographic criteria. All patients will require an intravenous cutdown to insure an adequate route for fluid administration. Fresh, type-specific whole blood, rather than packed cells or bank blood, is particularly important, both for the additional colloid provided as well as for clotting factors needed in the depleted baby. Preoperative platelet transfusion is rarely useful since the formed elements are rapidly destroyed in the peripheral circulation.

Adequate exposure of almost the entire abdominal cavity can be achieved through a right-sided supraumbilical transverse incision ex-

Figure 4. Stricture of the sigmoid colon as seen on a postevacuation barium enema. The roentgen findings mimic those of Hirschsprung's disease.

Figure 5. Chronic ulcer proximal to a stricture in the jejunum of a 3-month old baby who had pneumatosis during the first week of life.

tended to the left of the midline if necessary. We prefer to use plain catgut sutures for hemostasis, because nonabsorbable sutures can become septic. The risk of wound disruption is high in this group because of infection and severe catabolism. Therefore, all incisions are closed with internal, figure-of-eight, monofilament wire. We avoid through-and-through retention sutures if possible because of the proximity of exteriorized bowel and a gastrostomy tube.

The principles of any operation for NNE are: (1) resection of all grossly necrotic or perforated intestine; (2) preservation of the ileocecal valve and avoidance of extensive resection (i.e., upwards of 150 cm of small intestine) if at all possible. A "second look" operation at 24 hours is preferable to resecting long segments of questionably viable intestine; (3) exteriorization of all bowel ends either together as in a Mikulicz resection, or through separate openings on the abdominal wall. The temptation to close isolated perforations or perform end to end or other anastomoses should be avoided because of the increased risk of reperforation or anastomotic leakage and prolonged obstruction from edema and infection; (4) tube gastrostomy to minimize the risk of pulmonary aspiration and for feeding of the small premature baby during the postoperative period.

Total parenteral nutrition in the postoperative period is essential, particularly in the premature baby with exteriorized small intestine and in others with chronic diarrhea. This modality becomes safer if it can be

Table 2. *Results of Treatment of NNE at Yale-New Haven Hospital (July, 1973 to October, 1975)*

TREATMENT	NO.	ALIVE NO.	ALIVE (PER CENT)
No operation	10	4	(40)
Operation			
Acute with peritonitis	7	3	(40)
Late with stricture	3	2	(67)
TOTAL	20	9	(45)

withheld until intraabdominal sepsis is controlled. Specific bacteriology of intraperitoneal fluid cultures is important in selecting new or continuing the preoperative antibiotics. Re-establishing continuity of the gastrointestinal tract after exteriorization should await full recovery and positive nitrogen balance as evidenced by good weight gain. An extraperitoneal anastomosis is possible in patients having a Mikulicz exteriorization and is an additional advantage of this surgical approach.

Operative survival equals and occasionally exceeds that of purely medical treatment. Fifty percent of over 50 babies with acute NNE reported from four centers[32, 37, 42, 46] between 1955 and 1970 survived operation, while only 32 per cent recovered following medical treatment. This fact is particularly significant when considering that the sicker patients come to operation. The operative survival taken from more recent reports is even better. Twenty-one of 30, or 70 per cent of, patients operated on at the Denver Children's Hospital and University of Colorado between July of 1971 and June, 1974, recovered.[45] Our overall experience with acute NNE between July, 1973, and October, 1975 is summarized in Table 2. The improving survival with operative treatment is a reflection of better preoperative preparation, the earlier recognition of irreversible signs, and the supportive postoperative care, including the use of parenteral nutrition.

PATHOLOGY

There is considerable variability in the gross and microscopic findings. Lesions occur in all portions of the alimentary tract except the duodenum but the ileum and colon are by far the most commonly involved. The intestine is dilated, friable, and necrotic, often with areas of hemorrhage adjacent to frank zones of necrosis and seemingly viable intestine. Fibrin or exudate covers the serosal and peritoneal surfaces adjacent to a perforation. Perforations are usually seen in the ileocecal region where the intestinal wall is extremely thin. Formula may be clearly visible within the lumen. In 10 to 15 per cent of cases the entire bowel from stomach to rectum is discolored with varying degrees of frank necrosis and marginally viable intestine. I believe that gastric per-

Figure 6. Subserosal pneumatosis observed at autopsy in baby with diffuse nonperforated NNE.

forations, when accompanied by zonal necrosis, are another manifestation of NNE.[41]

Pneumatosis, while a common radiographic finding, is infrequently seen on gross inspection of the bowel at operation or autopsy. "Ballooning out" of the serosal surface is a sign of impending perforation and these areas may harbor an undetected zone of pneumatosis. Occasionally the entire bowel is necrotic and scattered pneumatosis is found in the subserosa (Fig. 6). Similarly, the bullae of pneumatosis are evident in the mucosal lining of the opened surgical specimen.

Localized perforation without obvious surrounding necrosis is an infrequent finding. Some believe these are "spontaneous,"[35] but most now agree that they represent very well localized full-thickness zones of necrosis, particularly if they are found in the ileum or colon. Seromuscular biopsies of the distal colon are indicated to rule out the enterocolitis of Hirschsprung's disease. Duodenal perforation without surrounding necrosis has been reported as a complication of nasojejunal feeding of the premature infant.[33] One should not confuse these traumatic lesions and similar localized perforations of the rectum[11] caused by a thermometer, enema, or catheter with the lesions of acute NNE.

The primary microscopic findings vary from individual to individual and with the progression of the disease. The earliest lesion is submucosal hemorrhage, edema, and ulceration seen alone or adjacent to frankly necrotic areas of the intestinal[15, 31, 32] wall (Fig. 7). Vascular engorge-

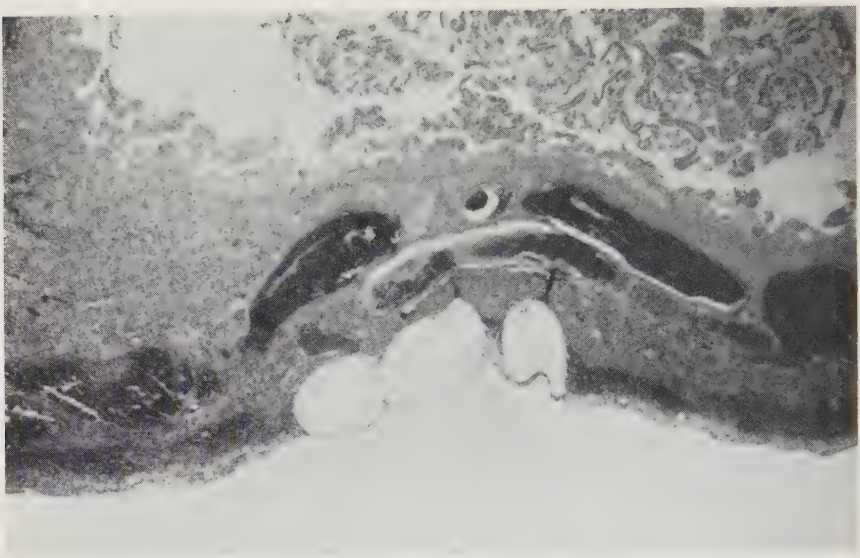

Figure 7. Subserosal pneumatosis, mucosal hemorrhage, and ulceration from baby with perforated necrotizing ileitis.

ment is also found in areas of interstitial hemorrhage. The ulcerated mucosa is often covered by a membrane of agglutinated inflammatory cells, necrotic epithelium, fibrin, and bacteria. Bland ischemic infarction of the entire thickness of the intestinal wall may be accompanied by only a minimal inflammatory response without hemorrhage.

Intramural ganglion cells are present, including the areas adjacent to the sites of necrosis and perforation. However, a causal relationship between acute NNE and the subsequent development of aganglionic megacolon has been raised in a recent report.[43]

Thrombi in mesenteric arterioles and venules are found on autopsy specimens but rarely at operation. This suggests that major vascular thrombosis is a late event, while the intramural vascular changes described above are a primary finding. The presence of vascular thrombosis at autopsy may also be a manifestation of disseminated intravascular coagulation, particularly when accompanied by intramural platelet fibrin thrombi. Diffuse hemorrhaging involving the brain, lungs, and pericardium is also a common postmortem finding and a further manifestation of a terminal coagulopathy.

Joshi et al[17] drew particular attention to the healing capacity of the intestine with NNE. They noted that epithelialization occurred as early as 3 days after the onset of NNE; the formation of granulation tissue and fibroplastic proliferation was seen within an 8 or 9 day period. Complete healing could lead to submucosal scarring and stricture formation. The resected specimen, including the stricture, is focally ulcerated and chronically inflamed; the stenotic zone is usually short, varying in length from 1 to 5 cm. A second stricture producing an intervening "enterocyst" has been reported.[24]

ETIOLOGY AND PREVENTION

Determining the etiology of NNE, its pathogenesis, and prevention has been one of the most exciting areas of research in neonatology during the past 5 years. Previous concepts including birth trauma,[47] congenital weakness or a defect in the intestinal wall,[10] bacterial enteritis subsequent to the ingestion of infected amniotic fluid,[3] a lysozyme-deficient diet,[26] or a localized Schwartzman reaction[14] have been discarded in favor of a dynamic alteration in the integrity of the mucosal cell by a number of different factors.

The most important of these factors are: (1) "selective circulatory ischemia" involving the mucosal cell; (2) a reduction or absence of the inherent protective immunologic activity (secretory IgA) in the gut of formula-fed babies; (3) colonization of the gastrointestinal tract during the first few days of life.

Lloyd[25] popularized the concept of "selective circulatory ischemia" as an asphyxial defense mechanism. This concept based on the "diving reflex" in aquatic mammals like the seal,[16] serves to protect the brain and heart from hypoxia by shunting blood away from the mesenteric, renal, and peripheral vascular bed. If one assumes that a similar reflex exists during delivery and in the immediate postnatal period, it is conceivable that an overshooting could occur in the stressed premature with hypoxia or hypothermia, causing ischemic changes that may eventually lead to necrosis or perforation. This hypothesis is supported by regional blood flow determinations in asphyxiated and resuscitated neonatal piglets.[39] Total gut perfusion and particularly mucosal perfusion as measured by the radio-rubidium distribution technique is dramatically reduced in the stomach, distal ileum, and colon during the asphyxial episode. The gut of resuscitated animals displayed a rebound in perfusion above normal (Fig. 8). Vascular congestion and mucosal hemorrhages observed in the ileum and colon of piglets are strikingly similar to the findings described in patients. In our opinion, these focal hemorrhages are the primary lesion in necrotizing enterocolitis and result from a combination of increased capillary fragility produced by gut ischemia and intramural vascular congestion in the resuscitated patient. Profound or prolonged ischemia may cause bland nonhemorrhagic infarction. In either case, focal mucosal necrosis, invasive bacterial proliferation, and transmural inflammation result in gastrointestinal dysfunction and contribute to the clinical findings of enterocolitis.

Umbilical venous catheters have also been implicated in the pathogenesis of NNE, particularly when the catheter tip is located in the portal system[39] rather than in the inferior vena cava. Portal venous pressure is significantly increased during the injection phase of experimental exchange transfusion via the umbilical vein of newborn piglets; transient portal venous hypertension is accompanied by a significant decrease in intramural colonic blood flow as measured by the radio-rubidium distribution technique. Umbilical artery catheters provide another vascular mechanism for causing NNE either by inducing vasospasm or by directly occluding the mesenteric artery with clot. Kitter-

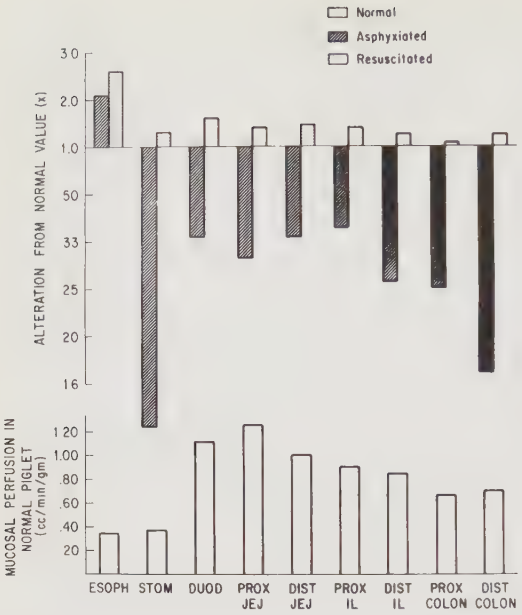

Figure 8. Mucosal perfusion of individual gut segments and alteration of values from normal in asphyxiated and resuscitated neonatal piglets. (Reproduced from Touloukian, R. J., Posch, J. N., and Spencer, R.: The pathogenesis of ischemic gastroenterocolitis of the neonate: selective gut mucosal ischemia in asphyxiated neonatal piglets. J. Ped. Surg., 7:194, 1972. Used with permission.)

man[18] believes that the usual cause of intestinal ischemia in a small premature infant is a patent ductus arteriosus with a large left-to-right shunt. His conclusions are based on data showing that the survival rate of babies having the conventional forms of medical therapy plus ligation of the PDA are superior to the usual medical and operative treatment. The significance of this report is difficult to assess because of the large number of variables being studied.

Hyperosmolar feedings have also been cited as causing further injury to the already sensitized mucosal cell in both animal and human studies. Prematurely delivered pigs fed hyperosmolar goat milk developed a disease closely resembling NNE.[5] Seven of eight babies under 1200 gm fed an elemental formula (Pregestimil, Mead Johnson Laboratories) having an osmolarity of 650 mOsm per L, developed the characteristic clinical features of NNE, and four required operation.[4] Herbst[13] showed that an increase in the concentration of reducing substances in the stool of a premature formula-fed baby using the Clinitest method actually precedes the clinically recognizable signs of acute NNE. This test, routinely used in all at risk babies, has obvious merit in the detection and prevention of its clinical manifestations.

A knowledge of the development of inherent immunity in the newborn gastrointestinal tract is essential to understanding the etiology of NNE and its subsequent prevention. The principal immunoglobulin in intestinal secretions is IgA; the vast majority of plasma cells present in the lamina propria of the gut are IgA-producing cells. The newborn infants lack secretory IgA for several days until food antigens and the endogenous flora of the colonized gut stimulate local antibody production. The primary source of IgA during these first few days is the colostrum

of mother's milk and, more specifically, the colostral leukocytes which provide passive immunity against enteric pathogens.[28] The protective effects of breast milk were convincingly demonstrated in experiments on paired groups of stressed newborn rats.[1] Nursing rats were uniformly protected against hypoxia, hypothermia, and Klebsiella feedings while formula-fed animals routinely developed necrotizing enterocolitis and died. Autopsy findings were consistent with that found in babies. Enteric overgrowth of potentially pathogenic bacteria in the formula-fed rat emphasizes the importance of intestinal flora in the pathogenesis of this disease. A key to the prevention of NNE now awaits results of ongoing studies determining the protective effect of the routine use of fresh breast milk in the susceptible baby.

REFERENCES

1. Barlow, B., Santulli, T. V., Heird, W. C., et al.: An experimental study of acute necrotizing enterocolitis—The importance of breast milk. J. Ped. Surg., *9*:587, 1974.
2. Bell, M. J., Kosloske, A. M., Benton, C., et al.: Neonatal necrotizing enterocolitis; prevention of perforation. J. Ped. Surg., *8*:601, 1973.
3. Blanc, W. A.: Amniotic infection syndrome: pathogenesis, morphology and significance in circumnatal mortality. Clin. Obstet. Gynec., *2*:705, 1959.
4. Book, L. S., Herbst, J. J., Atherton, S. O., et al.: Necrotizing enterocolitis in low birth weight infants fed an elemental formula. J. Pediat., *87*:602, 1975.
5. Delemos, R., Rogers, S. H., and McLaughlin, G.: Experimental production of necrotizing enterocolitis in newborn goats (Abst.). Ped. Res., *8*:380, 1974.
6. Denes, J., Gergely, K., Wohlmuth, G., et al.: Necrotizing enterocolitis of premature infants. Surgery, *68*:558, 1970.
7. Dickson, J. A. S.: Ross Conference on Pediatric Research: Necrotizing Enterocolitis in the Newborn Infant. Columbus, Ohio, Ross Labs., 1975, p. 13.
8. Donahoe, P. K., Stewart, D. R., Osmond, J. O., and Hendren, W. H.: Pneumoperitoneum secondary to pulmonary air leak. J. Pediat. *81*:797, 1972.
9. Dudgeon, D. L., Coran, A. G., Lauppe, F. A., et al.: Surgical management of acute necrotizing enterocolitis in infancy. J. Ped. Surg., *8*:607, 1973.
10. Fischer, A. E.: Fetal peritonitis: report of a case following spontaneous rupture of the large intestine. Am. J. Dis. Child., *36*:774, 1928.
11. Fonkalsrud, E. W., and Clatworthy, W.: Accidental perforation of the colon or rectum in newborn infants. N. Eng. J. Med., *272*:1097, 1965.
12. Frantz, I. D., III, L'Heureux, P., Engel, R., et al.: Necrotizing enterocolitis. J. Pediat., *86*:259, 1975.
13. Herbst, J. J.: Ross Conference on Pediatric Research: Necrotizing Enterocolitis in the Newborn Infant. Columbus, Ohio, Ross Labs., 1975, p. 71.
14. Hermann, R. E.: Perforation of the colon from necrotizing colitis in the newborn: report of a survival and a new etiologic concept. Surgery, *58*:436, 1965.
15. Hopkins, G. B., Gould, V. E., Stevenson, J. K., et al.: Necrotizing enterocolitis in premature infants. Am. J. Dis. Child., *120*:229, 1970.
16. Irving, L., Scholander, P. F., and Grinnel, S. W.: The regulation of arterial blood pressure in the seal during diving. Am. J. Physiol., *135*:557, 1942.
17. Joshi, V. V., Winston, Y. E., and Kay, S. Neonatal necrotizing enterocolitis. Am. J. Dis. Child., *126*:113, 1973.
18. Kitterman, J. A.: Ross Conference on Pediatric Research: Necrotizing Enterocolitis in the Newborn Infant. Columbus, Ohio, Ross Labs., 1975, p. 38.
19. Krasna, I. H., Becker, J. M., Schneider, K. M., et al.: Colonic stenosis following necrotizing enterocolitis of the newborn. J. Ped. Surg., *5*:200, 1970.
20. Krasna, I. H., Fox, H. A., Schneider, K. M., et al.: Low molecular weight dextran in the treatment of enterocolitis and midgut volvulus in infants. J. Ped. Surg., *8*:615, 1973.
21. Lee, S. B., and Kuhn, J. P.: Pneumatosis intestinalis following pneumomediastinum in a newborn infant. J. Pediat., *79*:813, 1971.
22. Leonidas, J. C., Krasna, I. H., Fox, H. A., et al.: Peritoneal fluid in necrotizing enterocolitis; a radiologic sign of clinical deterioration. J. Pediat., *82*:672, 1973.
23. Leonidas, J. C., Hall, R. T., Holder, T. M., et al.: Pneumoperitoneum associated with chronic respiratory disease in the newborn. Pediatrics, *51*:933, 1973.

24. Lloyd, D. A., and Cywes, S.: Intestinal stenosis and enterocyst formation as late complications of neonatal necrotizing enterocolitis. J. Ped. Surg., *8*:479, 1973.
25. Lloyd, J. R.: The etiology of gastrointestinal perforations in the newborn. J. Ped. Surg., *4*:77, 1969.
26. Mizrahi, A., Barlow, O., Berdon, W., et al.: Necrotizing enterocolitis in premature infants. J. Pediat., *66*:697, 1965.
27. Nuñez, R., and Mirambell, F.: Enterocolitis aguda necrosante. Rev. Med. Hosp. Nat. Ninos (Dr. Carlos Saenz Herrera), 9(1):1, 1974.
28. Pitt, J., Barlow, B., and Heird, W. C.: Macrophages and the protective action of breast milk in necrotizing enterocolitis. Ped. Res., *8*:384, 1974.
29. Reid, W. D., and Shannon, M. P.: Necrotizing enterocolitis: a medical approach to treatment. Can. Med. Assoc. J., *108*:573, 1973.
30. Rossier, A., et al.: L'enterocolite ulcero-necrotique du premature. Sem. Hop. Paris., *34*:1928, 1959.
31. Santulli, T. V., Schullinger, J. N., Heird, W. C., et al.: Acute necrotizing enterocolitis in infant: a review of 64 cases. Pediatrics, 55:376, 1975.
32. Stevenson, J. K., Oliver, T. K. J., Graham, C. B., et al.: Aggressive treatment of neonatal necrotizing enterocolitis: 38 patients with 25 survivors. J. Ped. Surg., 6:28, 1971.
33. Sun, S. C., Samuels, S., Lee, J., et al.: Duodenal perforation: a rare complication of neonatal nasojejunal tube feeding. Pediatrics, 55:371, 1975.
34. Tan, K. L., Tan, A. Y. O., and Wong, T. T. T.: Necrotizing enterocolitis in young infants. Clin. Ped., *11*:44, 1972.
35. Thelander, H. E.: Perforation of the gastrointestinal tract of the newborn infant. Am. J. Dis. Child., 58:371, 1939.
36. Torma, M. J., DeLemos, R. A., and Rogers, J. R.: Necrotizing enterocolitis in infants. Analysis of forty-five consecutive cases. Am. J. Surg., *126*:758, 1973.
37. Touloukian, R. J., Berdon, W. G., Amoury, R. A., et al.: Surgical experience with necrotizing enterocolitis in the infant. J. Ped. Surg., 2:389, 1967.
38. Touloukian, R. J., Posch, J. N., and Spencer, R.: The pathogenesis of ischemic gastroenterocolitis of the neonate: selective gut mucosal ischemia in asphyxiated neonatal piglets. J. Ped. Surg., 7:194, 1972.
39. Touloukian, R. J., Kadar, A., and Spencer, R. P. The gastrointestinal complications of neonatal umbilical venous exchange tranfusion: a clinical and experimental study. Pediatrics, *51*:36, 1973.
40. Touloukian, R.: Ischemic gastrointestinal lesions in the neonate. Paediatrician, 3:230, 1974.
41. Touloukian, R.: Gastric ischemia: the primary factor in neonatal perforation. Clin. Ped., *12*:219, 1973.
42. Touloukian, R.: Ischemic gastroenterocolitis in infants: clinical aspects and thoughts on its etiology. Conn. Med., *37*:229, 1973.
43. Touloukian, R. J., and Duncan, R.: Acquired aganglionic megacolon in a premature infant. Pediatrics, 56:459, 1975.
44. Virnig, N. L., and Reynolds, J. W.: Epidemiological aspects of neonatal necrotizing enterocolitis. Am. J. Dis. Child., *128*:186, 1974.
45. Wayne, E. R., Burrington, J. D., and Hutter, J.: Neonatal necrotizing enterocolitis. Evolution of new principles in management. Arch. Surg., *110*:476, 1975.
46. Wilson, S. E., and Woolley, M. M.: Primary necrotizing enterocolitis in infants. Arch. Surg., *99*:563, 1969.
47. Zillner, E.: Ruptura flexurae sigmoidis neonati inter partum. Arch. Anat. Path. (Paris), *96*:307, 1884.

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Esophageal Atresia and Tracheoesophageal Fistula Malformations

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The embryologic development of the trachea and esophagus has been studied by many but the mechanisms of malformation which result in esophageal atresia and tracheoesophageal fistula deformities are still not clear. At about the 21st day of embryonic development the foregut begins to form into the dorsal esophagus and the ventral trachea. The two organs are separated by a process of septation beginning at about the carina and extending cranially toward the larynx. It is believed by some that an interruption in the septation process between days 24 and 28 would result in a fistula between the esophagus and the trachea. An early "interruption" would thus result in a lower fistula while a disturbance in the septation process occurring later might result in a higher fistula. The reader is referred to the excellent article by Smith[29] and to the chapter by Hopkins[16] for more details on embryology.

It is in any case suggested that the disturbance which produces these esophageal deformities is a generalized one because frequently associated with esophageal atresia are vertebral anomalies, cardiac lesions, duodenal atresia, imperforate anus, and genitourinary anomalies. All of these organ systems appear to be developing rapidly at the time that the esophagus and trachea are dividing, lending evidence to the concept that a systemic insult to the embryo is responsible.

Although there have been sporadic cases of siblings being born with esophageal atresia, it is also true that one member of a set of twins may be affected while the other is normal. There is no known pattern of heritability.

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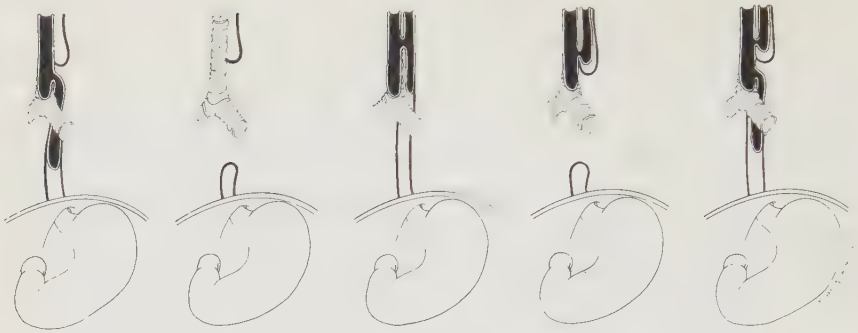

Figure 1. The various types of esophageal atresia (EA) and tracheoesophageal fistula (TEF) malformations are illustrated along with their relative incidence according to the "Survey."[14] The group of esophageal atresia with both proximal and distal TEF may be considerably larger than illustrated here (see text). (Figs. 1 and 5 from Holder, T. M., and Ashcraft, K. W.: Esophageal atresia and tracheoesophageal fistula. *In* Hardy, J. D. (ed.): Rhoads Textbook of Surgery, 5th ed. Philadelphia, J. B. Lippincott Co., in press.)

ANATOMY

Esophageal atresia (EA) and tracheoesophageal fistula (TEF) may occur as separate deformities but they occur together most commonly (Fig. 1). Classification of the possible lesions in order to simplify communication has resulted in perhaps 12 or more schemes. The confusion resulting from these classifications has led us to use an anatomically descriptive scheme that requires no previous familiarity with the lesion or the literature. Those patients having esophageal atresia may have the isolated lesion or may have a co-existing fistula from one or both ends of the atretic esophagus to the trachea. Those patients having a tracheoesophageal fistula may have the isolated lesion as well.

The most common form of the abnormality is esophageal atresia with distal tracheoesophageal fistula (EA with distal TEF). This easily understood class is also known as type 3, VII, IIIb, III, IV, 3c, C, A, B, E, and 1 depending upon whose particular classification is being used. Isolated esophageal atresia is similarly known as type 2, VII, II, I, A, B, and D. The advantage of the anatomic descriptive method should be obvious.

Considerable data regarding the malformation come from a survey taken of the members of the Surgical Section of the American Academy of Pediatrics and reported in 1964[14] (hereinafter called the "survey"). This survey included 1058 patients representing much of the combined experience of many pediatric surgeons of the United States and Canada. It does not include the notable large series of Cameron Haight nor the smaller series reported and not reported by a number of pediatric and thoracic surgeons scattered throughout the country. According to the survey, 86.5 per cent of patients had EA with distal TEF, nearly 8 per

cent had isolated EA, 4 per cent had isolated TEF, and about 1 per cent had EA with proximal TEF and EA with TEF from both proximal and distal esophagus. Our personal experience and that of others now suggest that EA with proximal and distal TEF may account for probably 4 to 5 per cent of the patients.[5] The extra patients are probably ones that were originally classified as EA with distal TEF. Some of these patients were thought to have a recurrent TEF postoperatively when the second fistula was discovered.

In addition to the obvious esophageal and tracheal abnormalities, concomitant lesions occur with some frequency. The most common of these associated lesions are congenital heart disease, gastrointestinal abnormalities, and skeletal and muscular deformities.[25] A recognizable abnormality is diagnosed in probably 50 per cent of the patients who have esophageal atresia and/or tracheoesophageal fistula. In addition to these obvious anatomic abnormalities, approximately 35 per cent of patients with EA and TEF will be born premature by weight or age.

DIAGNOSIS

The actual incidence of esophageal atresia and TEF abnormalities is difficult to assess. It is probably near 1 in 3000 births. This makes it one of the most frequent anomalies which, if not treated, will be uniformly fatal in the neonatal period. There are two conditions which may herald the birth of a child with esophageal atresia—hydramnios and prematurity. It is felt that hydramnios is associated very frequently with high, obstructive gastrointestinal lesions which prevent effective swallowing and absorption of the amniotic fluid. Waterston has demonstrated that the incidence of polyhydramnios is 85 per cent in patients with esophageal atresia who do not have a distal TEF and 32 per cent in those patients who do have this communication. This suggests that the TEF serves as an in utero conduit for ingested amniotic fluid. Whether or not the hydramnios associated with esophageal atresia will lead to premature labor is open to question. Eastman and Hellman feel that it probably is a precipitating factor in the early parturition. At any rate, prematurity occurs in about 8 per cent of births in the United States but is found in 34 per cent of children with esophageal atresia and distal tracheoesophageal fistula. Prematurity and polyhydramnios are signs which probably warrant specific steps to exclude esophageal atresia as will be discussed below.

Ultimately, of course, the purpose in early diagnosis is to avoid the complications of aspiration and regurgitation pneumonitis. If one is able to make the diagnosis within several hours of birth, the likelihood of severe pneumonitis developing prior to definitive treatment is much reduced. It is important to recognize those patients who are presumably at risk of having esophageal atresia and do whatever is necessary to confirm or exclude the lesion. In addition to prematurity and polyhydramnios, actual symptoms of the lesion may be recognized. What is thought to be excessive mucus is probably not really excessive, except that all the saliva the child forms is regurgitated and none of it is swallowed.

This is perhaps the earliest of symptoms of the lesion. It is important that nursery personnel be aware of this symptom and understand the necessity to communicate their suspicions freely to the attending physician. These same nurses are in the best position to recognize that these children cough, choke, regurgitate, and at times become cyanotic when being fed. The recognition of these symptoms, of course, calls for immediate complete evaluation. There are some patients whose first symptoms of esophageal atresia will be respiratory—usually pneumonitis. This occurs most commonly in the right upper lobe but may sometimes extend from that area.

Diagnostic Method

In the infant suspected of having esophageal atresia with or without tracheoesophageal fistula, a stiff, radiopaque, well lubricated 10–14 French catheter should be passed through either nostril or through the mouth in an attempt to reach the stomach. If the catheter meets an obstruction at 9 to 13 cm from the nares, the diagnosis of esophageal atresia is made. An x-ray of the chest to include the abdomen should then be taken. This can be a simple, portable, upright film which will record the level to which this catheter is passed, its position, the status of the lungs, the contour of the heart, the presence of gross vertebral anomalies, and whether or not there is air in the intestine to indicate a patent distal TEF (Fig. 2). It is not really necessary to introduce any contrast material into the upper esophageal pouch for confirmation. It is indeed probably completely unnecessary and perhaps dangerous to these children to undergo fluoroscopy for diagnosis of this lesion. Should contrast x-ray be desired, 0.5 ml of barium instilled carefully into the upper esophageal pouch with a second plain portable chest x-ray in the upright position will suffice.

DIAGNOSTIC ERRORS. There are several diagnostic pitfalls to be avoided. The most serious error is probably the selection of a very small, flexible catheter to pass as a means of excluding esophageal atresia. These soft small caliber tubes will coil easily in the upper esophageal pouch to give one the impression of having passed into the stomach. By contrast, in using a stiff, large caliber plastic catheter it is often possible to observe the tube coiling in the stomach through the anterior abdominal wall after its passage. This will obviate the need for even taking a chest x-ray to determine the depth of passage of the tube unless the patient has obvious interference with his phonation. (In that case it is likely that the tube has passed through the vocal cords and may well have gone through a distal tracheoesophageal fistula to reach the stomach. Although this has been recorded rarely, it is a distinct possibility and one to be considered.)

Another maneuver which seems to appeal to the novice is the injection of air into the catheter while listening with a stethoscope over the upper abdomen and assuming that the bubbling sound produced will be proof that the tube has passed into the stomach. It is not surprising that the child cries during these maneuvers which force air through his distal tracheoesophageal fistula. A bubbling sound is thus produced to give an erroneous impression. Aspiration of bile-stained material by way of

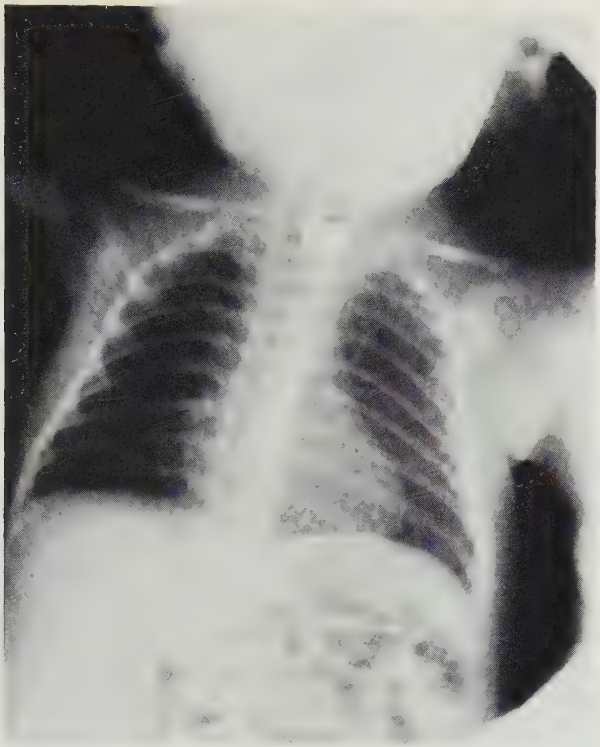

Figure 2. X-ray with sump suction tube and barium in proximal pouch to show atresia, presence of air in the gut, status of lungs, skeletal system, and cardiac silhouette.

the nasogastric tube has frequently been interpreted as being evidence that the tube has passed into the stomach. It is not that difficult for an infant with EA and distal TEF to regurgitate bilious material into his trachea, cough it into the pharynx, and swallow it into the upper pouch, from which it is removed by suction. One can certainly avoid these pitfalls by using a large, stiff tube. There is little danger in the large tube for the obstruction is definite and the very muscular upper pouch seems to resist perforation.

The child who has esophageal atresia and no distal TEF will, in addition to having the blind ending proximal esophagus, have no air in the intestine on x-ray (Fig. 3). It is extremely unusual for the patient with distal TEF to have a gasless abdomen, although Haight has reported that, in his experience, about 1.5 per cent of patients will resemble isolated esophageal atresia.

The diagnosis of isolated TEF (without atresia) is often difficult to make or exclude as the case may require. Symptoms in the neonate —coughing and choking with drinking and recurrent pneumonitis —are often insidious. Because not all demonstrate spillage through the TEF each time they swallow, the contrast radiograph is not the best means of making or excluding this lesion. When the TEF is demonstrated radiographically the problem is solved (Fig. 4). If contrast is

Figure 3. Esophageal atresia without fistula. Barium outlines of proximal pouch. There is considerable pneumonitis present. Note the "gasless" abdomen.

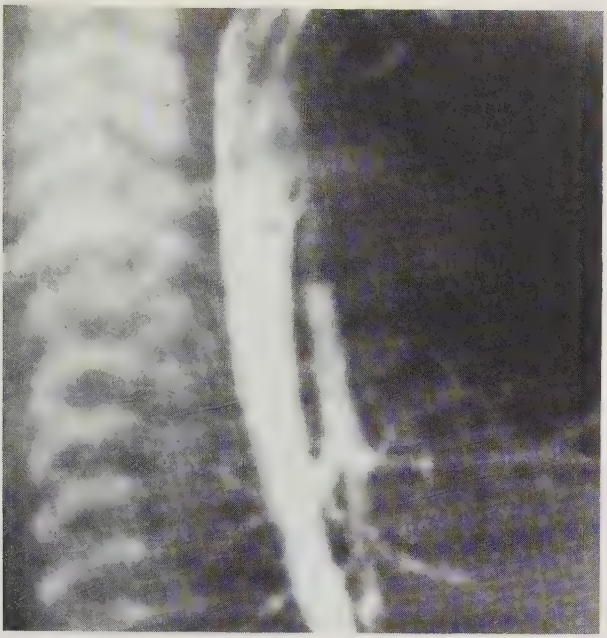

Figure 4. Isolated tracheoesophageal fistula.

noted in the trachea without seeing the TEF, the question of spillover is raised. Of considerable help is the ancillary radiographic finding of poor peristalsis in the esophagus below the fistula.[31]

Bloating is another symptom of isolated TEF. This occurs as a result of swallowing air forced through the TEF by crying.

Careful endoscopy with specialized equipment is usually the most reliable diagnostic method for isolated TEF. Bronchoscopy may be all that is needed.[9] Occasionally the instillation of methylene blue dye into an endotracheal tube with positive pressure will allow the fistula to be observed through the esophagoscope.

PATHOLOGIC PHYSIOLOGY

Although unable to effectively swallow saliva and milk, the child with esophageal atresia accumulates liquid in the upper esophageal pouch. This may either spill over and be aspirated into the airway or may produce marked upper airway obstruction because of impingement upon the soft posterior upper trachea. If there is an upper pouch fistula the possibility of the swallowed material entering the airway is greatly enhanced.

Regurgitation of gastric acid via the distal tracheoesophageal fistula is probably the most dangerous pathogenetic process in this disorder. Contributing to the likelihood that this will occur is the fact that the child will close his glottis while crying, forcing air through the TEF and

down into the stomach. Relief of the gastric distention back into the esophagus allows reflux of acid or bile into the airway. This will produce a rather severe chemical pneumonitis which is usually located in the right upper lobe. The chemical pneumonitis very likely gives way to a bacterial pneumonitis (given enough time and the usual contamination from tubes and feedings). Additionally, gastric and intestinal dilatation may elevate the diaphragms to such an extent that respiration is impaired. Although the stomach cannot adequately be decompressed without a gastrostomy, it is probably true that placing the child in an infant seat at about 45° will at least minimize the chance of liquid in the stomach refluxing into the trachea.

The child with isolated TEF swallows air forced through the fistula into the esophagus. Bloating results which may promote reflux up into the esophagus and the trachea. Since the esophagus is intact, all regurgitated material is not necessarily shunted into the airway and episodes of aspiration pneumonia tend to be sporadic and less severe.

For some unknown reason esophageal peristalsis is deficient in children who have either esophageal atresia with distal tracheoesophageal fistula or isolated TEF. This feature is of some diagnostic help in the isolated TEF. Difficulty in swallowing, particularly with poorly masticated food, allows this to become a prominent symptom even after division of the TEF. This problem may simulate anastomotic stricture in the repaired atresia. Such patients choke, regurgitate, and otherwise do not handle solids and semi-solids very well because of this abnormality.[21, 27]

TREATMENT FOR ESOPHAGEAL ATRESIA AND TRACHEOESOPHAGEAL FISTULA

Preoperative Treatment

The aim of a period of preoperative treatment in the patient with esophageal atresia and tracheoesophageal fistula is to improve the child's chance of surviving operative correction and the postoperative period. Obviously the baby who has clear lungs and no source of sepsis is going to fare better than one who has extensive pneumonitis if both are to undergo a major operative procedure. Not only does this period of preoperative preparation allow treatment of existing acute pathologic processes such as pneumonitis but it includes the prevention of further deterioration and the evaluation and, perhaps, concomitant treatment of other abnormalities. This would include the treatment of idiopathic respiratory distress syndrome, cardiac failure due to congenital heart disease, or other lesions which might interfere with the immediate operative approach to the esophageal atresia. Very low birth weight is one of these lesions. The risk classification of Waterston, Bonham-Carter, and Aberdeen gives some indication of the value of a period of careful preoperative care.[36] Their Group A consists of term infants who have negligible pneumonitis and no other abnormalities. Survival rate in this category is expected to be 95 per cent or better. Group B consists of infants whose birth weight is between 1800 and 2500 gm who are other-

wise well. This group would also include larger infants who have moderate pneumonitis or some notable but not life-threatening concomitant anomalies. Survival rate in this group is 68 per cent. Obviously, if only low birth weight is the problem, increasing the birth weight must reduce risk. Certainly, improving pulmonary function would increase the ability of the lungs to withstand definitive repair. Waterston's Group C includes all infants whose birth weight is extremely low or who are severely ill or who have life-threatening concomitant anomalies. It may only be possible to partially improve these patients but in many instances a period of careful preoperative planning and attention to other disorders will place the child into Group B rather than in Group C.

Details of this preoperative care period are described elsewhere[13] but consist basically of gastrostomy for decompression, continuous suction of the blind upper pouch, elevation, evaluation and management of other problems such as congestive heart failure, and perhaps treatment of the idiopathic respiratory distress syndrome (Fig. 5). The idea that a child has to be above 1800 or 2000 gm prior to his repair is no longer as important as it was once considered since the survival of 1800 gm babies without other lesions is now rather routine.

Gastrostomy is the most important aspect of the preoperative treatment of any patient with EA and TEF. One cannot insure the lowest incidence of gastroesophageal reflux with chemical pneumonitis short of doing a gastrostomy. It is a safe, simple procedure which can be done under local anesthesia. The excellent gastric decompression provides a considerable margin of safety during this preoperative period. It is extremely useful also as a means of postoperative feeding while allowing the esophageal anastomosis to heal.

A sump suction tube remains the most efficient means of keeping

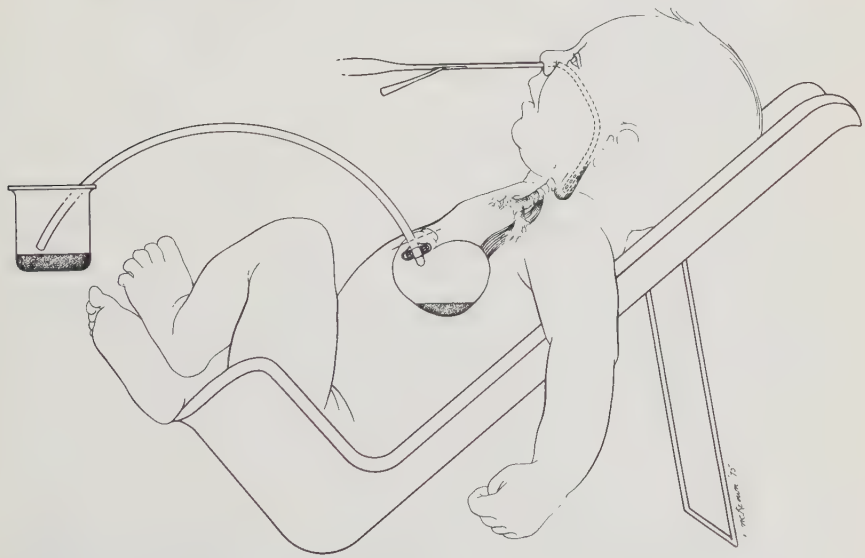

Figure 5. Preoperative care is administered in the semi-Fowlers position with proximal pouch sump drainage and gastrostomy decompression.

the proximal pouch free of secretions until time of repair.[26] Nursing care during this period of preoperative treatment is of the utmost importance. A nurse who is alert and aware of the potential problems and who will keep both the gastrostomy and the sump suction tube functioning will be of immeasurable help in this process.

Operative Treatment

The definitive primary operative procedure for patients with esophageal atresia and a distal tracheoesophageal fistula is division of the fistula and esophageal anastomosis. Done through a right thoracotomy, it is safer to use the extrapleural approach minimizing the problems which may occur with esophageal anastomotic leak (Fig. 6*A*).[12] Recognizable leaks at the anastomosis occur in about 10 to 20 per cent of patients.[14] The extrapleural method does require a few minutes more operating time but the potential benefit to the child is worth it. The distal TEF is located and surrounded with an umbilical tape (Fig. 6*B*). This effectively shuts off air leak through the fistula. The distal esophagus should not be mobilized more than absolutely necessary. Certainly none of the small feeding blood vessels which come in from the mediastinum should be divided. The fistula is divided and the trachea is oversewn with fine silk (Fig. 6*C*). The upper pouch is mobilized well up into the neck of both to insure that there is not a second fistula from the upper pouch to the back wall of the trachea and to allow for anastomosis without undue tension (Fig. 6*D*). The maneuver is facilitated by placing a stiff No. 20–24 French catheter into the esophageal pouch with which the anesthesiologist can stretch the upper pouch downward while the dissection is being carried out. Traction sutures may also be used to pull the proximal pouch down. An anastomosis is made between the upper pouch and the distal esophagus without removing any of the distal esophagus. There is a considerable disparity in the size of the proximal and distal esophagus. Either done by halves or quadrants the anastomosis can be created in such a way as to allow for this disparity. We have done both the Haight two-layer anastomosis (Fig. 6*E*) (bringing the second suture line down over the first as a protection against leak) and the single-layer end-to-end anastomosis, which tends to leak a little more often but produces fewer anastomotic strictures. A tube is left in the extrapleural space and brought out below the incision through a separate stab wound (Fig. 6*F*). Should a leak occur the saliva will drain through this extrapleural tube. The intact pleura prevents emphysema should a leak occur. At about the 10th day this extrapleural tube can be removed.

In 1951, Sulamaa et al.[30] described primary repair done by ligation of the fistula and end-to-side esophagoesophagostomy. They felt the procedure to be of value in the patient with a short proximal pouch. Having more problems with symptoms of recurrent TEF than in those patients whose TEF was ligated, the authors recommended this technique only in unusual circumstances of a large gap.

Ty, Brunet, and Beardmore[34] reported in 1967 their experience with a series of patients preferentially treated in this way. As of 1973 Beardmore had 35 patients operated upon by this method with four having recurrent TEF and eight anastomotic strictures. Touloukian[33] has reported

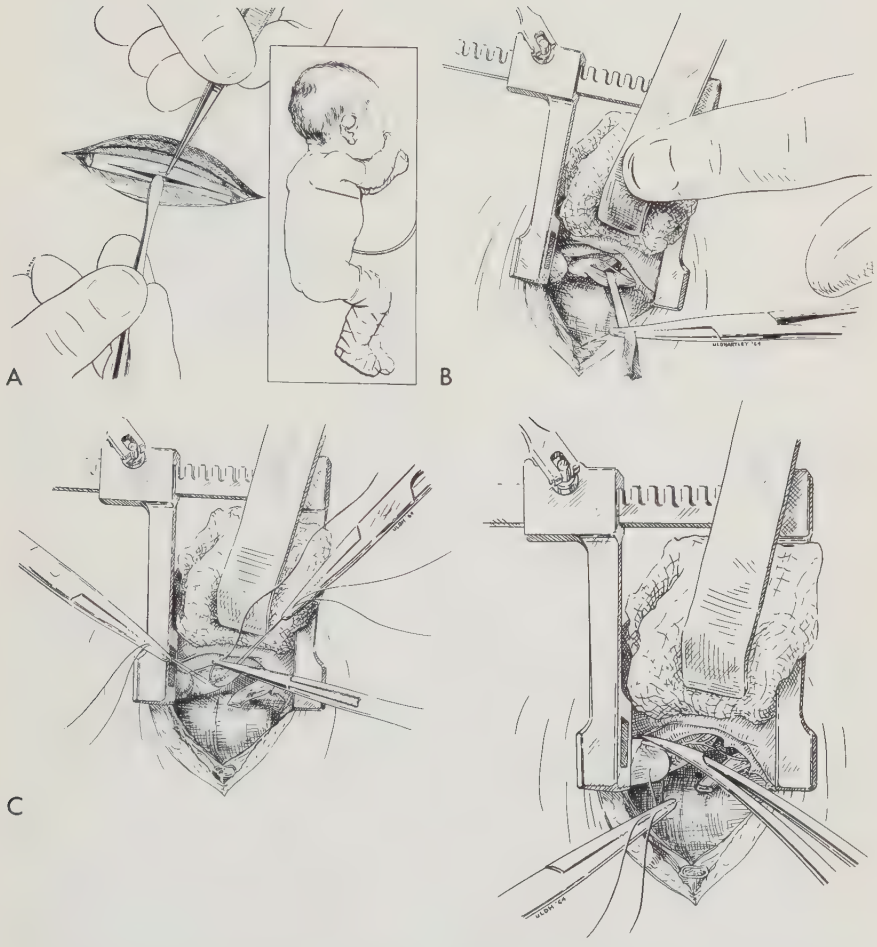

Figure 6. *A*, The position of the baby for definitive repair of esophageal atresia is illustrated. The extrapleural approach is best done by subperiosteal rib resection developing the space between endothoracic fascia and pleura by blunt and sharp dissection. *B*, The distal esophagus is encircled with an umbilical tape to stop the anesthetic leak into the stomach. *C*, Division of the fistula at the membranous tracheal wall allows closure with fine silk sutures of the tracheal wall. The distal esophagus is not handled or mobilized further. *D*, Dissection of the upper esophageal pouch is facilitated by a traction suture in the apex or by having the anesthetist push on a large catheter in the pouch.

(*Legend continued on the opposite page*)

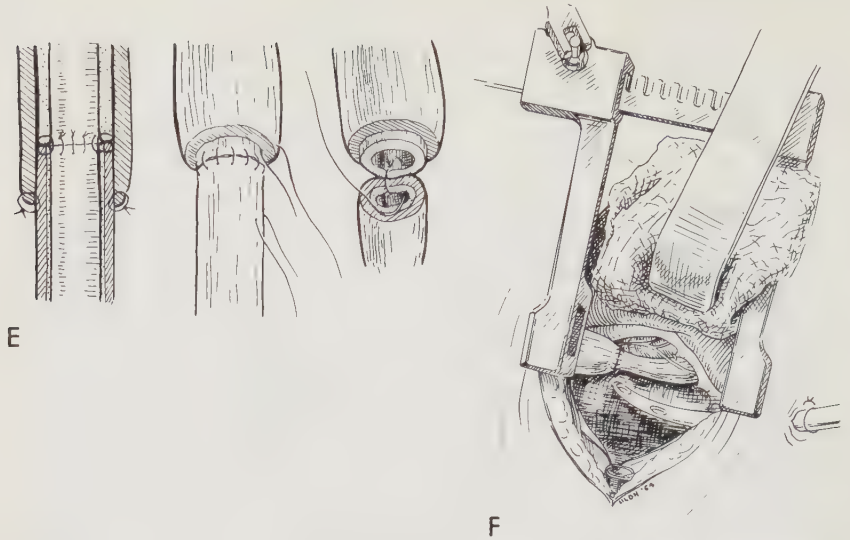

Figure 6 *Continued.* *E*, The Haight two-layer technique for esophageal anastomosis. *F*, The completed anastomosis with an extrapleural tube placed so as not to touch the suture line. (Reproduced from Holder, T. M., and Ashcraft, K. W.: Esophageal atresia and tracheoesophageal fistula. Curr. Probl. Surg., Aug. 1966. Used with permission.)

18 patients done by this technique with one TEF and no strictures. Leix and Schwab had eight patients with one recurrent TEF.[22]

In a series of 38 patients, however, operated upon by four pediatric surgeons at Toronto's Hospital for Sick Children, 19 were operated upon using the technique popularized by Beardmore and 19 were done conventionally.[6] In the 19 patients with the end-to-side repair there were eight anastomotic leaks and 11 strictures. There were four leaks and six strictures in the comparable group of end-to-end repairs. Seven end-to-side ligated fistulae recurred.

Thus, totaling these reported 80 patients we see that there were 13 recurrent TEF (16 per cent).

In those children who have esophageal atresia and distal tracheoesophageal fistula but who are extremely ill with pneumonitis or have other anomalies, it is wise to devote a good bit of time to the preoperative care. Nutrition can be provided by way of central or peripheral vein as long as the pulmonary status is not deteriorating in the face of an open distal tracheoesophageal fistula. This is sometimes very helpful while one is managing an imperforate anus or severe urinary tract abnormality or an intestinal atresia in preparation for the definitive esophageal operation.

"Staging" or the division of a tracheoesophageal fistula without complete repair[17, 20] has undergone considerable metamorphosis during the last several years. This is due partly to the fact that most surgeons who are doing these operations routinely have gained considerable skill both in the respiratory and surgical aspects of their operative treatment and accept lower weights at primary repair. The necessity of having to undergo esophageal fistula division without primary repair may now be obviated by using gastrostomy decompression as a means of prevention

of further pulmonary problems coupled with parenteral alimentation for nutrition.[15] The child thus "delayed" no longer needs two major operative procedures.[2, 8] The very small, very ill babies with associated problems are probably still best treated by extrapleural division of the distal tracheoesophageal fistula and later anastomosis of the esophagus.

ISOLATED ESOPHAGEAL ATRESIA

What might be called the *standard* approach to the child with isolated esophageal atresia consists of gastrostomy for feeding purposes immediately upon diagnosis. The upper esophageal pouch is brought to the skin as an esophagostomy in the suprasternal notch. Between 6 months and a year an esophageal substitution procedure may be carried out. Our preference has generally been for the substernal interposition of right colon. This has the disadvantage that there is no natural gastroesophageal junction. Reflux into the colon segment may produce ulceration of the colonic mucosa (6 per cent in our experience). Dilatation of the anastomosis at the sternal notch and at the cologastrostomy is difficult because of position and inability to pass a rigid esophagoscope into the stomach. Substernal colon interposition has the distinct advantage of being an extrapleural procedure. It is relatively simple to do and it is quite effective. An anastomotic leak at the upper end (which unfortunately occurs with some frequency) is usually well tolerated and produces only a local short-term drainage.

Waterston prefers to use transverse or left colon interposed via a left thoracotomy into the gap between the esophageal ends.[35] The natural gastroesophageal junction will theoretically prevent reflux and peptic ulcer in the colon segment. Unfortunately anastomotic leak cannot help but result in empyema which may be fatal. Some surgeons now have gone to gastric tube esophagoplasty, constructing a tube from the greater curvature of the stomach which may be placed in a substernal position or in the left pleural space to join with the proximal esophagus. We have not used this procedure. It has the theoretical disadvantage of reducing the capacity of the stomach and has the advantages that only one end-to-end anastomosis is required and that it probably will not elongate and dilate as the colon segment is sometimes noted to do.

As an alternative to an interposition, Howard and Myers introduced in 1961 the technique of elongation of the upper pouch in isolated atresia to allow primary anastomosis.[18] Nineteen patients have been reported as having successfully undergone this method of treatment.[23, 32] Only a few have had mechanical elongation of the lower esophageal segment because of the problem in insertion of the bougie. More than half had anastomotic leaks and more than half had problems with stricture. Several patients have required resection of stricture and reanastomosis. Hendren has reported two patients in whom magnetic metal bougie olives were placed in proximal and distal esophageal pouches.[11] The child's crib is placed in an electromagnetic field with current being supplied 90 seconds and off for 60 seconds. Both children have sub-

sequently undergone primary anastomosis with satisfactory results. One patient required 45 days of such bougienage and one 30 days.

Although extremely expensive, bougie elongation of the esophagus has the theoretical advantage of a "normal" esophagus to serve esophageal function. In point of fact the peristalsis in this esophagus is frequently poor and anastomotic stricture is often difficult to manage. Colon interposition and gastric tube esophagoplasty are both somewhat plagued by short and long-term complications. The surgeon must select the technique best suited to his situation and experience.

ISOLATED TRACHEOESOPHAGEAL FISTULA

Operative division of isolated tracheoesophageal fistula is almost always done by the right supraclavicular approach to avoid injury to the thoracic duct as it empties into the venous system on the left.[1, 19] It may be helpful to endoscope the child and pass a ureteral catheter through the fistula for ease in identification but that is not a necessity. The fistula is generally found higher than one would imagine. Both ends are closed over with interrupted silk sutures. It is only rare that an isolated tracheoesophageal fistula will be located so low that it has to be approached through the chest. Approach via the pleural space is advised in this instance with a closure of the fistula in the standard manner. The transpleural approach is safe for this lesion because one does not have the high incidence of leaks that occur with a full circumferential anastomosis of the esophagus.

POSTOPERATIVE COMPLICATIONS

Esophageal anastomotic leak is probably the most serious complication to occur after operation on patients with esophageal atresia.[7] If the anastomosis has been done extrapleurally, the leak is generally well tolerated. The exception to this is the patient who cannot be fed by gastrostomy because of massive gastroesophageal reflux and in whom a significant portion of the colonic intake is lost through the extrapleural drain. Leaks usually occur from the 7th to the 10th day following anastomosis. They are generally small and they generally close spontaneously. There may be some reaction about the anastomotic leak which will subsequently produce stricture but in our experience this has not been a predictable sequel. Most patients will tolerate a small leak very well as long as feeding by gastrostomy is possible. After the leak stops draining the chest tube may be removed. Such patients should be watched a little more carefully for subsequent stricture.

An esophageal leak into the pleural space is always a more serious and even potentially lethal complication.[36] The soiling of the pleural space frequently will require take-down of the anastomosis, treating the patient thereafter as if he had isolated esophageal atresia. This, of course, is a devastating setback. For these reasons we advocate the extrapleural approach for repair of esophageal atresia.

Esophageal strictures are relatively common after anastomosis. This

may be due to a rather tenuous blood supply or to excessive handling of tissues (which tends to produce interference with blood supply and with healing). Stricture also may be due to inflammatory reaction after anastomotic leak or recurrent irritation of the anastomosis by refluxed gastric content. Most anastomotic strictures may be managed with one or two dilatations. Troublesome strictures warrant careful investigation for gastroesophageal reflux.[24] Should gastroesophageal reflux be found in this situation then an appropriate treatment plan should be instituted. A hiatus hernia in a child who has undergone repair of esophageal atresia is unlikely to resolve by postional therapy alone because the esophagus is under some tension. It is necessary in these instances to go ahead with fundoplication to relieve reflux. In the absence of a demonstrable hiatus hernia it may be worthwhile to position the baby hoping that gastroesophageal junction integrity will develop in time.

There are two abnormalities which are not complications of repair of esophageal atresia and tracheoesophageal fistula deformities. These are altered peristalsis in the distal portion of the esophagus and an abnormal cry or cough. Peristalsis disturbances consist primarily of lack of tertiary stripping which propels food down the esophagus and into the stomach. Bread and meat seem to be particularly difficult to swallow for these children. At first it was thought that this phenomenon might be due to denervation from operation. The same problem is noted in the patients with isolated tracheoesophageal fistula who have not undergone repair. Disordered peristalsis has also been noted in patients who have not had the distal esophagus divided from the trachea prior to anastomosis of the upper and lower segments after the method of Sulamaa. It is a troublesome and aggravating but not often a serious problem.

In addition to the altered esophageal motility, children with esophageal atresia often have an abnormal voice. These children have a cat-like cry or a barking cough, both of which have been self-limiting in our experience. These children grow up to talk quite normally.

RESULTS

Because there are so many factors which influence the survival of a child with esophageal atresia and tracheoesophageal fistula malformations, it is difficult to assess a risk for any given patient. Although compiled some 12 years ago, the survey of the Surgical Section of The American Academy of Pediatrics is probably still broad enough to encompass the many variables and give a valid picture of the problem. In this survey of 1058 patients the overall mortality was 39 per cent. This included all types of tracheoesophageal malformations, all sorts of associated congenital anomalies in 505 of the patients, and a variety of surgeons working in a variety of institutions. Interestingly, there was little difference in survival between those patients treated in a children's hospital and those patients treated in a general hospital. Considering the common form of the anomaly in 478 patients with no associated defects, 78 per cent survived. When the patient had a congenital heart lesion associated with EA and TEF only 22 per cent survived. Genitourinary anomalies resulted in a similar survival rate in

a smaller number of patients. Imperforate anus carried a 43 per cent survival, while associated intestinal atresia found only 13 per cent of patients surviving. Interestingly, of 350 patients with the common type of malformation who died, 208 were assessed to be unavoidable and included respiratory problems which we would not now consider to be necessarily unavoidable deaths. This included idiopathic respiratory distress syndrome and severe pneumonia. There were 88 avoidable deaths and 57 deaths in which an error was made by the doctor while in 10 instances an error by the nurse accounted for the patient's demise. Perhaps the ensuing 12 years have lessened considerably the mortality from these factors. We do know that extreme prematurity and complex associated abnormalities sometimes make survival virtually impossible by today's standards. For example, of 44 patients with isolated tracheoesophageal fistula, 32 per cent died. By most any measure today the child with isolated esophageal atresia should expect 100 per cent survival precluding severe associated abnormalities.[4]

Although much credit must go to Cameron Haight for the success of this procedure, many others had given their experience in the years between the original description of the lesion and the development of a successful primary operation for it. Indeed many improvements have occurred since Cameron Haight's remarkable accomplishment in 1941. The development of better general pediatric care, safer anesthesia, and gentler operative techniques, and experience with the lesion have reduced complications and mortality in this lesion. It has been estimated that 400 patients with esophageal atresia abnormalities were recorded in the literature prior to the first survivor and we know that there must be several thousands who have been treated since that time. Accordingly, the patient who survives operation at present owes some debt of gratitude to the innumerable surgeons who have been able to improve bit by bit upon the surgical approach for this lesion.

REFERENCES

1. Aberdeen, E.: Congenital tracheoesophageal fistula without esophageal atresia. *In* Rab, C. (ed.): Operative Surgery, 2nd ed. London, Butterworths, 1968.
2. Abrahamson, J., and Shandling, B.: Esophageal atresia in the underweight baby: a challenge. J. Ped. Surg., 7:608–613, 1972.
3. Ashcraft, K. W., and Holder, T. M.: The story of esophageal atresia and tracheoesophageal fistula. Surgery, 65:332–340, 1969.
4. Bond-Taylor, W., Starer, F., and Atwell, J. D.: Vertebral anomalies associated with esophageal atresia and tracheoesophageal fistula with reference to the initial operative mortality. J. Ped. Surg., 8:9–13, 1973.
5. Dudgeon, D. L., Morrison, C. W., and Woolley, M. M.: Congenital proximal tracheoesophageal fistula. J. Ped. Surg., 7:614–19, 1972.
6. Ein, S. H., and Theman, T. E.: A comparison of the results of primary repair of esophageal atresia with tracheoesophageal fistulas using end-to-side and end-to-end anastomosis. J. Ped. Surg., 8:641–45, 1973.
7. Eraklis, A. J., and Gross, R. E.: Esophageal atresia management following an anastomotic leak. Surgery, 60:919–923, 1966.
8. Firor, H. V., Pildes, R., and Vidyasagar, D.: Delayed repair of esophageal atresia with T. E. fistula in two premature infants: use of a jejunostomy as an alternative to intravenous alimentation. J. Thorac. Cardiov. Surg., 66:828–832, 1973.
9. Gans, S. L., and Berci, G.: Inside tracheoesophageal fistula: new endoscopic approaches. J. Ped. Surg., 8:205–211, 1973.
10. Gibson, T.: The Anatomy of Humane Bodies Epitomized, 6th ed. London, Awnsham and Churchill, 1703.

11. Hendren, W. H., and Hale, J. R.: Lengthening of esophageal segments in congenital esophageal atresia by electromagnetic bougienage, N. Eng. J. Med., 293:428–432, 1975.
12. Holder, T. M.: Transpleural versus retropleural approach repair of tracheoesophageal fistula. SURG. CLIN. N. AM., 44:1433–1439, 1964.
13. Holder, T. M., and Ashcraft, K. W.: Esophageal atresia and tracheoesophageal fistula. Curr. Probl. Surg., August, 1966.
14. Holder, T. M., Cloud, D. T., Lewis, J. E., Jr., and Pilling, G. P., IV: Esophageal atresia and tracheoesophageal fistula: A survey of its members by the Surgical Section of the American Academy of Pediatrics. Pediatrics, 34:542–549, 1964.
15. Holder, T. M., Leape, L. L., and Mann, C. M., Jr.: Esophageal atresia, tracheoesophageal fistula and associated anomalies: Hyperalimentation as an aid in treatment. J. Thorac. Cardiovasc. Surg., 63:838–840, 1972.
16. Hopkins, W. A.: The esophagus. *In* Gray, S. W., and Skandalakis, J. E. (eds.): Embryology for Surgeons. Philadelphia, W. B. Saunders Co., 1972.
17. Holder, T. M., McDonald, V. G., Jr., and Woolley, M. M.: The premature or critically ill infant with esophageal atresia: increased success with a staged approach. J. Thorac. Cardiovasc. Surg., 44:344–358, 1962.
18. Howard, R., and Myers, N. A.: Esophageal atresia: a technique elongating the upper pouch. Surgery, 58:725–727, 1965.
19. Killen, D. A., and Greenlee, H. B.: Transcervical repair of H. type congenital tracheoesophageal fistula: review of the literature. Ann. Surg., 162:145–150, 1965.
20. Koop, C. E., and Hamilton, J. P.: Atresia of the esophagus: increased survival with staged procedures in the poor-risk infant. Ann. Surg., 162:389–401, 1965.
21. Laks, H., Wilkinson, R. H., and Schuster, S. R.: Long-term results following correction of esophageal atresia with tracheoesophageal fistula: a clinical and cinefluorographic study. J. Ped. Surg., 7:591–597, 1972.
22. Leix, F., and Schwab, C. E.: End to side operative technique for esophageal atresia with tracheoesophageal fistula. Am. J. Surg., 118:225–235, 1969.
23. Mahour, G. H., Woolley, M. M., and Gwin, J. L.: Elongation of the upper pouch and delayed anatomic reconstruction in esophageal atresia. J. Ped. Surg., 9:373–383, 1974.
24. Pieretti, R., Shandling, B., and Stephens, C. A.: Resistant esophageal stenosis associated with reflux after repair of esophageal atresia: a therapeutic approach. J. Ped. Surg., 9:355–357, 1974.
25. Quan, L., and Smith, D. W.: The VATER association: Vertebral defects, Anal atresia, T-E fistula with esophageal atresia, Radial and Renal dysplasia: a spectrum of associated defects. J. Pediat., 104:7, 1973.
26. Replogle, R. L.: Esophageal atresia plastic sump catheter for drainage of the proximal pouch. Surgery, 54:296–297, 1963.
27. Shepard, R., Fenn, S., and Sieber, W. K.: Evaluation of esophageal function in postoperative esophageal atresia and tracheoesophageal fistula. Surgery, 59:608–617, 1966.
28. Sloan, H.: Cameron Haight, in memoriam. J. Thorac. Cardiovasc. Surg., 62:479–480, 1971.
29. Smith, E. I.: The early development of the trachea and esophagus in relation to atresia of the esophagus and tracheoesophageal fistula. Contr. Embryol. Carnegie Inst. Wash. #245, 36:41, 1957.
30. Sulamaa, M., Gripenberg, L., and Ahvenainen, E. K.: Prognosis and treatment of congenital atresia of the esophagus. Acta Chir. Scand., 102:141, 1952.
31. Thomas, P. S., and Chrispin, A. R.: Congenital tracheoesophageal fistula without esophageal atresia. Clin. Radiol., 20:371–374, 1969.
32. Thomasson, B. H.: Congenital esophageal atresia: mercury bag stretching of the upper pouch in a patient without tracheoesophageal fistula. Surgery, 71:661–663, 1972.
33. Touloukian, R. J., Pickett, L. K., Spackman, T., and Biancani, P.: Repair of esophageal atresia by end-to-side anastomosis and ligation of the tracheoesophageal fistula: a critical review of 18 cases. J. Ped. Surg., 9:306–310, 1974.
34. Ty, T. C., Brunet, C., and Beardmore, H. E.: A variation in the operative technique for the treatment of esophageal atresia with tracheoesophageal fistula. J. Ped. Surg., 2:118–126, 1967.
35. Waterston, D. J.: Reconstruction of the esophagus. *In* Mustard, W. T., Ravitch, M. M., Snyder, W. H., Jr., Welch, K. J., and Benson, C. D. (eds.): Pediatric Surgery. Chicago, Year Book Medical Publishers, Inc., 1969.
36. Waterson, D. J., Bonham-Carter, R. E., and Aberdeen, E.: Oesophageal atresia: Tracheoesophageal fistula. A study of survival of 218 infants. Lancet, 1:819, 1962.

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Congenital Posterolateral Diaphragmatic Hernia

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Clamping the umbilical cord at birth precipitates a number of complicated physiologic adaptive changes in the newly born infant. Perhaps the most critical of these is the sudden alteration of the means whereby blood is oxygenated and carbon dioxide is excreted. During embryonic and fetal development this transfer is accomplished via the placental circulation. At birth gas exchange must be assumed by the infant's lungs.

The infant born with a congenital posterolateral diaphragmatic hernia has less functioning pulmonary parenchyma than does the normal infant.[4, 7, 21] Almost all of the pathophysiologic sequelae in infants with a sizeable posterolateral diaphragmatic hernia are due to poorly functioning lungs. The goal is to maximize the function of the existing pulmonary parenchyma. If the surgeon focuses on this objective, rather than the anatomic repair of the diaphragmatic hernia, the various modes of therapy will assume rational priority. Anatomic correction of the diaphragmatic hernia itself is a relatively simple task. Management of the metabolic derangements, however, are more complex.[3, 18]

EMBRYOGENIC DEVELOPMENT OF DIAPHRAGMATIC HERNIA (INCOMPLETION OF DIAPHRAGM)

The posterolateral congenital diaphragmatic hernia is commonly referred to by the eponymic label "Bochdalek's hernia." Although this term is firmly entrenched by common usage there is a serious question as to accuracy of this label because of Bochdalek's original description and concept of this type of hernia.[1, 2] He referred to the hernia as being due to a separation of the muscular fibers, implying that this was perhaps a disruption of the existing diaphragm during embryologic development. It now appears to be rather well established that this hernia is

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simply due to the persistence of a normally occurring hiatus in the diaphragm known as the pleuroperitoneal canal.[15, 22, 23] In the normal sequence of embryologic development the pleuroperitoneal canal is the last diaphragmatic hiatus to close. The closure is completed during the 7th or 8th week of intrauterine development. Closure of the canal completes the rather complex development of the diaphragm. If the canal does not close completely prior to the migration of the intestine from the umbilical cord into the peritoneal cavity (at approximately 12 weeks' gestation), the bowel can migrate through the pleuorperitoneal canal into the chest cavity. The defect is on the left side in about 75 per cent of patients and on the right in 25 per cent.

Displacement of the intestine, part of the liver, and commonly the spleen results in a space-occupying lesion of the left hemithorax. This inhibits growth of the left lung by direct mechanical pressure.[4, 7, 17] Inhibition of the pulmonary growth and development is directly proportional to the volume of viscera which are displaced into the hemithorax. On rare occasions a defect is present in the diaphragm at birth with herniation of the bowel into the chest at a later date. If this is the case, the underlying lung is normal in size but atelectatic.[24] The vast majority of patients, however, appear to have the bowel in the chest cavity for a period of time during intrauterine development, causing significant lung hypoplasia.

The continuing high mortality rate resulting from this lesion is due to two basic causes: (1) lack of early recognition (on occasions the diagnosis is made at autopsy); (2) inadequate functioning pulmonary parenchyma. (This accounts for a significant mortality, even when early diagnosis is established and optimal treatment instituted.)[5, 6, 8, 11, 14, 16, 20]

DIAGNOSIS

Physical Findings

In contrast to some congenital anomalies, which occur by genetic predisposition, maternal age, or in association with hydramnios, there is no consistent prepartum warning of the impending delivery of an infant with posterolateral diaphragmatic hernia. The first indication of the presence of this anomaly is usually cyanosis soon after the umbilical cord is clamped. If enough abdominal viscera are in the chest, the abdominal contour may be abnormally scaphoid in remarkable comparison to a barrel-shaped thorax. The heart is shifted to the right hemithorax in the left posterolateral diaphragmatic hernia so that the cardiac sounds are best heard in the right chest. The consistent tetrad of physical findings associated with left congenital diaphragmatic hernia are: (1) early cyanosis, (2) scaphoid abdomen, (3) barrel-shaped chest, and (4) dextrocardia. Audible peristaltic sounds in the affected hemithorax are a very unreliable physical finding. Peristaltic sounds are readily transmitted from the peritoneal cavity through the chest wall so that this theoretically is an interesting finding, but is of little pragmatic value.

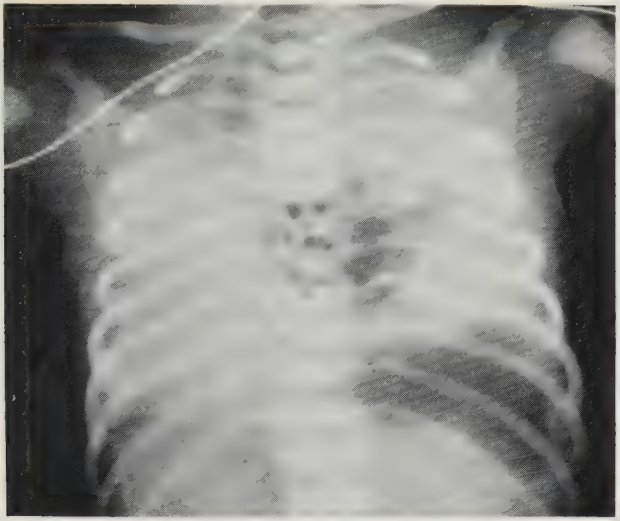

Figure 1. Chest roentgenogram of infant with left posterolateral diaphragmatic hernia. The loops of bowel containing fluid and gas are seen in the left hemithorax.

Roentgenographic Findings

Any infant with neonatal respiratory distress should have a chest roentgenogram performed as early as is possible. The appearance of congenital diaphragmatic hernia on a simple posteroanterior chest roentgenogram is usually quite characteristic (Fig. 1). If the chest roentgenogram leaves no doubt as to the diagnosis as well as the side of the lesion, then therapy can be instituted immediately. In some patients

Figure 2. Chest roentgenogram of infant with cystic adenomatoid malformation of the right lung. This causes mediastinal shift to the left but there is no bowel gas pattern extending into the thoracic cavity.

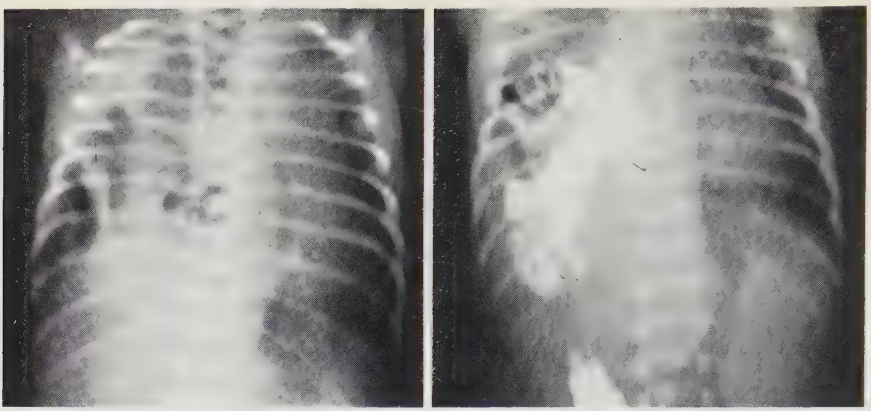

Figure 3. If there is any question as to the etiology of the gas filled structure in the thorax, opaque medium may be introduced into the stomach. In this case the gas is contained within loops of bowel which are later identified by intraluminal barium.

the x-ray appearance may be similar to that of cystic adenomatoid malformation of the lung and it is particularly important to differentiate between the two (Fig. 2). Diaphragmatic hernias are most commonly corrected through an abdominal incision. Cystic adenomatoid lobes require thoracotomy for definitive therapy. If the chest x-ray is equivocal, one can repeat the film with a nasogastric tube in place. If the tube is opaque and indicates that the stomach is in the chest, a diagnosis of diaphragmatic hernia is established. If any question remains, opaque medium may be introduced into the stomach via a nasogastric tube. In the case of diaphragmatic hernia, the opaque material will find its way into the viscera in the thoracic cavity, and in the case of cystic adenomatoid malformation the opaque medium will outline a normal infradiaphragmatic visceral pattern (Fig. 3).

A neonate has a potentially lethal lesion with posterolateral diaphragmatic hernia. Although severe respiratory distress may not be present initially, sudden decompensation and death can occur with tragic rapidity. All therapy, therefore, should proceed with dispatch.

PREOPERATIVE EVALUATION, RESPIRATORY SUPPORT, AND MEDICAL THERAPY

Nasogastric Tube Decompression

Since it is desirable to decrease the size of the space-occupying lesion in the patient's chest, a nasogastric tube should be positioned in the patient's stomach and the stomach emptied by intermittent aspiration. By this simple but important maneuver the size of the stomach is diminished and it prevents further gut distention.

Respiratory Assistance

Any respiratory assistance needed should be given through an endotracheal tube; using a mask can force some gas through the esophagus

into the stomach, thus increasing the size of the space-occupying lesion in the thoracic cavity.

Transportation

If the patient must be transported from one hospital to another, this should be accomplished as rapidly as is possible with the nasogastric tube, and possibly an endotracheal tube, in place. If the chest x-ray accompanies the infant, valuable time can be saved. Another chest x-ray need not be taken at the receiving hospital. The infant can be admitted directly to the operating room where the forewarned team can proceed with definitive therapy.

Laboratory Studies

In addition to the routine blood count, an initial Astrup acid-base study will aid in evaluation and therapy. Serial Astrup blood studies may be performed during the operative procedure to determine the efficacy of the therapy. Optimally, arterial blood should be obtained through an arterial cannula; however, if this is not immediately available one may use capillary blood from the warmed heel of the infant. The usual abnormalities include a decreased blood pH (frequently below 7.0), elevated Pco_2, as well as a negative base excess and perhaps a decreased Po_2.[3, 18]

THERAPY

Although the therapy will be described under three general headings, i.e., medical, anesthetic, and surgical, this is for didactic reasons only. The therapeutic measures are implemented simultaneously.

Medical Therapy

Since the infant with diaphragmatic hernia is being perfused with poorly oxygenated, hypercarbic blood, respiratory as well as metabolic acidosis is frequently well established.[18] The metabolic acidosis is treated with intravenous administration of sodium bicarbonate using the following formula: weight (in kilograms) $\times$ negative base excess $\times$ .03 = the number of milliequivalents of sodium bicarbonate to be administered. It is generally considered safest to administer one-half of this amount by intravenous push, then to re-evaluate the infant with the Astrup study prior to administering the remainder of the sodium bicarbonate at a slower rate, depending upon the serial Astrup results.

If laboratory studies are not immediately available and the clinical condition suggests acidosis, one may safely proceed with the administration of 1 to 3 mEq of sodium bicarbonate per kg of body weight. Optimally, however, the sodium bicarbonate should be titrated by serial Astrup blood studies.

Anesthetic Management

If an endotracheal tube has not been inserted prior to the patient's arrival in the operating room, an endotracheal tube is inserted and taped securely in place. Usually this can be accomplished without an anes-

thetic agent or relaxant. If the infant is vigorous enough to resist the intubation, D-tubocurare (0.25 mg per kg) can be administered to relax the infant for intubation. An air-oxygen mixture, using 40 per cent oxygen, is administered and small amounts of Halothane may be added if the infant is vigorous and resisting. Frequently the air-oxygen mixture is all that is necessary or desirable, particularly during the early minutes of operation. It is critical for the anesthesiologist to be aware of the limitations of expansion of the lungs. If too much endotracheal pressure is applied both lungs can be ruptured, further decreasing the functioning pulmonary parenchyma. Ventilatory pressure should be kept below 20 cm of water. The ipsilateral lung specifically is allowed to expand gradually rather than by force.

Surgical Technique

Although posterolateral diaphragmatic hernias can be repaired either through an abdominal or thoracic incision, we prefer the abdominal approach for several reasons (Fig. 4). The hernia can be reduced readily through an abdominal incision. While the assistant retracts the bowel away from the diaphragm, repair can be accomplished without the pressure of bowel against the diaphragm. Additionally, if the abdominal incision is used, one has the option of producing a ventral hernia or of even placing a Silon cover over the bowel if the peritoneal cavity cannot be closed without undue intraperitoneal pressure.[19] Malrotation is consistently associated with the hernia. It can be corrected readily through the abdominal incision. Gastrointestinal decompression is most effectively accomplished by means of a Stamm gastrostomy, also done more easily through an abdominal incision. An inherent danger of blind reduction of the bowel through a thoracic incision is the possibility of producing a midgut volvulus.[6]

The exact type of abdominal incision, whether transverse, oblique, or vertical, is a matter of personal preference. The vertical rectus muscle splitting incision is adequate. It can be made quickly and affords adequate exposure for the operative procedure. This is our incision of choice in the majority of patients (Fig. 4*a*).

After the peritoneal cavity is opened, one can visualize the posterolateral diaphragmatic defect; by gentle traction the viscera are pulled into the abdominal incision (Fig. 4*b*). A catheter may be placed through the defect into the thoracic cavity to break a vacuum and aid reduction; however, in my personal experience this is an unnecessary maneuver. By gentle traction on one segment of intestine at a time, the bowel is readily reduced from the thoracic cavity into the peritoneal cavity and one can visualize the defect with ease (Fig. 4*c*). Spectators are often amazed at the volume of viscera which have occupied the hemithorax. They commonly include part of the stomach, all of the small intestine, all of the large intestine except the left colon, the left lobe of the liver, and the spleen. After the hernia is completely reduced the anesthesiologist will notice less resistance to ventilatory assistance.

If the anterior leaf of the diaphragm is retracted anteriorly with a retractor, the left lung can be seen. If it is a small, solid lappet, one can an-

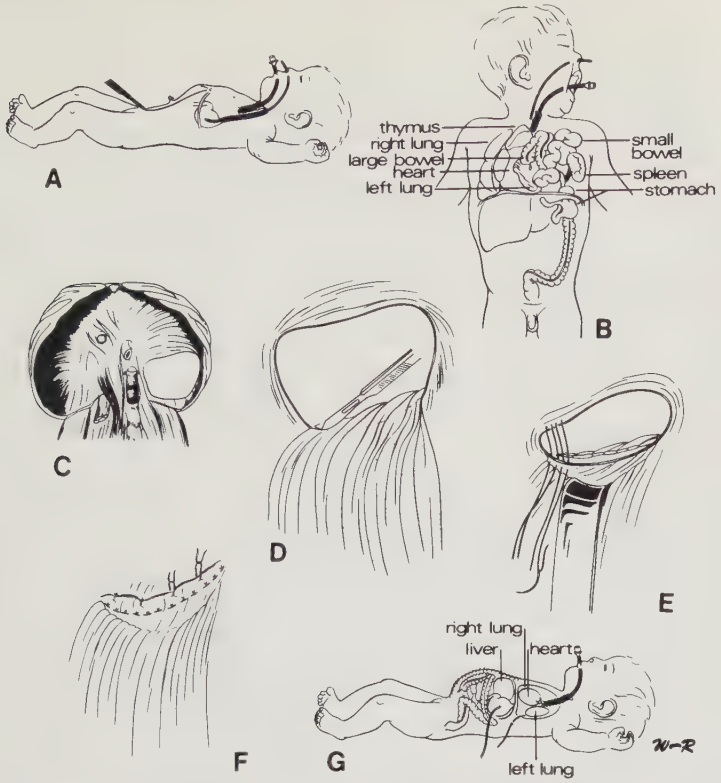

Figure 4. *A*, Nasogastric tube in place. Surgical incision left paramedian. *B*, Viscera lie within the left hemithorax, thus pushing the mediastinal structures to the right and collapsing both lungs. *C*, Location of left posterolateral diaphragmatic defect. *D*, Incision of pleuroperitoneum to isolate posterior rim of diaphragmatic muscle. *E*, First sutures placed to overlap the diaphragmatic muscle. *F*, Second layer of silk sutures placed in diaphragmatic defect. *G*, Termination of operation showing ventral hernia, gastrostomy, chest tube, and endotracheal tube in place for postoperative respiratory assistance.

ticipate continuing respiratory insufficiency. If the lung is initially small and atelectatic but expands readily and assumes a reasonable size, the eventual outlook for adequate pulmonary function is better. A frequent observation is that of a small lung which expands partially. It is tempting to manually inflate the lung by positive pressure ventilation. This temptation must be resisted because it can rupture one or both lungs. The lungs should be allowed to expand gradually without too much assistance.

In observing the ipsilateral lung, the surgeon must note whether or not he is seeing the lung through a diaphanous serous membrane or not. Since the membrane is frequently very thin and compressed against the underlying lung, it can be overlooked easily. The best maneuver to settle the question is to actually manipulate the lung with a pair of surgical forceps. If a membrane is present it should be removed; otherwise it can fill with serosanguinous fluid postoperatively, resulting in a space-occupying lesion in the chest.[10] Before beginning closure of the defect, a pleural catheter is introduced through a stab wound in the left chest.

This is positioned posteriorly for adequate drainage of fluid and air in the postoperative period. Once the chest catheter has been placed and the hernia sac, if present, has been removed, the diaphragmatic defect can be closed.

In the majority of infants the defect in the diaphragm is not very large and there is adequate diaphragmatic substance for closure. The anterior rim of the diaphragm is quite evident; however, the posterior rim may not be apparent and may require dissection for delineation (Fig. 4*d*). If the underlying kidney is retracted downward by the assistant, the surgeon can incise the pleuroperitoneum over the posterior muscular rim. Gentle dissection can usually define a rim of muscle medially, posteriorly, and, less frequently, laterally. Medially the defect may approach esophageal hiatus, but rarely does it actually involve the hiatus itself. There is usually a small rim of muscle between the defect and the hiatus. Rarely, there is inadequate diaphragmatic tissue and one must resort to using muscle flaps developed from the anterior abdominal wall and chest wall or to inserting a prosthetic cloth such as Dacron.[9, 20]

In the majority of infants in whom the diaphragmatic tissue can be approximated as a definitive closure, it is our preference to overlap the anterior and posterior diaphragmatic layers with interrupted 3–0 silk (Fig. 4*e*). Sutures are first passed through the posterior rim from caudad to cephalad, then through the free edge of the anterior rim and back through the posterior rim so that the surfaces are securely apposed. A second layer of silk may then be placed through the free edge of the posterior rim into the anterior diaphragmatic substance (Fig. 4*f*). This affords a secure closure and recurrence of diaphragmatic hernia should be very rare.

Attention is then turned to the duodenum where Ladd's bands are lysed so that the duodenum can be visualized from the stomach to the jejunum. Of course, there is no ligament of Treitz.

A gastrostomy is performed with a no. 18 Depezzar mushroom catheter placed in the stomach through three concentrically placed purse string sutures of 4–0 silk. The catheter is exited through a separate stab wound to the left of the incision.

If persistent respiratory insufficiency is anticipated, a catheter should be placed into the aorta through an umbilical artery for postoperative gas monitoring. It is safest to have the catheter tip in the aorta below the renal arteries to avoid possible renal or mesenteric emboli.

The method of closure of the abdominal wall depends upon the intraperitoneal pressure which is produced thereby. One can manually stretch the abdominal wall to enlarge the peritoneal cavity. If closure is easy, an anatomic layer closure can be performed. In the majority of patients, the degree of increased intraperitoneal pressure will significantly compromise the pulmonary function. Therefore, it is desirable to leave a ventral hernia either by closure of skin only or by a Silon pouch.[19] If skin closure is performed, it is desirable to place a sheet of Silon plastic over the bowel to prevent troublesome adhesions. After all evidence of respiratory insufficiency has passed, the ventral hernia can be corrected.

POSTOPERATIVE CARE

Although no attempt should be made to expand the ipsilateral lung during the operative procedure, if it does expand without undue endotracheal pressure one can anticipate a less troublesome postoperative course than if the ipsilateral lung is solid and airless at the end of the operation.

The chest tube is placed to water seal drainage without suction. This allows the lung to expand at its own rate and provides drainage of serosanguinous fluid from the chest cavity. If suction is added to the chest tube drainage, there is danger of excessive pressure being transmitted to the pulmonary parenchyma resulting in rupture of the lung. In calculating the effective alveolar pressure, one must add the positive endotracheal tube pressure to the negative chest tube pressure. We feel it is simpler and safer to not have negative pressure applied to the chest tube.

The gastrostomy is placed to drainage and is irrigated with air at frequent enough intervals to assure patency.

Respiratory sufficiency or insufficiency is determined by serial arterial blood gas studies. If possible the Po_2 is kept between 50 and 60 mm of mercury. The percentage of inhaled oxygen is best kept below 60 per cent; however, if oxygenation is inadequate at this level the concentration can and should be increased along with the institution of positive end expired pressure of 2 cm of water. The maximum pressure should not exceed 25 cm of water and if possible should be kept below 20 centimeters of water. If PEEP is used, the blood pressure must be monitored carefully because of the possibility of decreasing venous return to the heart due to the positive pressure within the thoracic cavity.

Metabolic acidosis, if present, is treated with intravenous sodium bicarbonate using the same formula which was referred to earlier, i.e.: weight (in kilograms) $\times$ negative base excess $\times 0.3 =$ the number of milliequivalents of sodium bicarbonate to be administered. After administering one-half of the sodium bicarbonate the base excess can be reevaluated prior to administration of the remainder of the sodium bicarbonate. In this way overtreatment can be avoided.

Temperature control throughout the clinical course is of critical importance. At all times the ambient temperature must be kept at a level to have a normothermic baby. Although an isolette can be used, nursing care within an isolette is more difficult. Currently we use the Olympic warming hood* which allows easy access to the infant and to all the catheters and tubes attached to the patient.

A chest roentgenogram should be taken immediately after the operation and is repeated depending upon the patient's clinical course. Lung expansion and location of the endotracheal tube are the two major factors to be followed on the serial chest roentgenograms. If the endotracheal tube is placed too far down in the trachea, one or the other of the mainstem bronchi are obstructed. This should be corrected promptly.

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*Olympic Medical Corporation, Seattle, Washington.

Antibiotic therapy for the neonate who undergoes major surgical correction is usually indicated for a few days. The type of antibiotics to use depends upon the major bacterial flora which are present in the nursery at the time.

If the infant survives for 48 hours postoperatively he has an excellent chance of eventual survival. If the above therapeutic measures are instituted with dispatch and with skill and the infant does expire within the first 48 hours, usually there is inadequate pulmonary parenchyma for life support.

COMMUNICATION WITH PARENTS

Although the pediatrician and surgeon are most concerned about the care of the critically ill infant, good medical care and human concern include appropriate and timely communication with the parents. Of course the mother is hospitalized, frightened, and anxious when the infant has been taken from her in an abrupt fashion and hospitalized elsewhere. If she is fortunate enough to have a concerned and emotionally stable husband, the surgeon can explain the nature of the anomaly and the anticipated prognosis to the father. He can in turn communicate appropriately with his wife. If the mother is single or if the father is temporarily or permanently incapable of handling this responsibility, the surgeon should communicate with the mother either in person, through the family physician, or by telephone. It is now well recognized that prolonged separation of the infant from its mother is destructive to the mother-infant bonding. As soon as is possible the mother should be encouraged to visit and care for the infant in the hospital.

If the infant does not survive, an autopsy should be requested in order to best explain the infant's death to the parents. Their most common question, either spoken or unspoken, is "Did I do something wrong to produce this problem in my infant?" This question implies both concern and possibly deep feelings of guilt. Someone on the medical team should be able to help the parents with this debilitating attitude. It is my opinion that frequently the surgeon is in the best position to offer this help, but as long as it is accomplished by some member of the medical or surgical team in an empathic, knowledgeable fashion, it matters not exactly who it is. It is, however, imperative that it be accomplished.

SUMMARY

The infant who is born with a posterolateral diaphragmatic hernia who becomes symptomatic at or soon after birth requires urgent care. Surgical reduction of the diaphragmatic hernia must be accomplished quickly. Respiratory and metabolic acidosis must be treated appropriately. The parents should be informed of the gravity of their infant's problem and reassured by appropriate explanation of the nature of the defect and the therapeutic requirements. If the infant dies, the parents

are in need of empathy, reassurance, and adequate explanation so that they do not have lingering doubts regarding the etiology of the anomaly and the adequacy of the therapy. If the infant lives, the medical team can share the feeling of a job well done.

REFERENCES

1. Bochdalek, V. A.: Einige Betrachtungen über die Entstehung des angeborenen Zwerchfellbruches. Als Beitrag zur pathologischen Anatomie der Hernien. Vierteljahrschr. f.d. prakt. Heilk., *19*:89, 1848.
2. Bochdalek, V. A.: Praktische Bemerkungen über Zwerchfellbruche nebst Beschreibung eines mit einer Fraktur der Lendenwirbelsaule komplizierten Falles. Vierteljahrschr. f.d. prakt. Heilk., *94*:14, 1867.
3. Boix-Ochoa, J., Peguero, G., Seijo, G., Natal, A., and Canals, J.: Acid-base balance and blood gases in prognosis and therapy of congenital diaphragmatic hernia. J. Ped. Surg., *9*:49, 1974.
4. Campanale, R. P., and Rowland, R. H.: Hypoplasia of the lung associated with congenital diaphragmatic hernia. Ann. Surg., *142*:176, 1955.
5. Carter, P. E. B., Waterston, D. J., and Aberdeen, E.: Hernia and eventration of the diaphragm in childhood. Lancet, *1*:656, 1962.
6. Collins, D. L., Pomerance, J. J., Travis, K. W., Turner, S. W., and Pappelbaum, S. J.: A new approach to congenital posterolateral diaphragmatic hernia. Presented at the Annual Meeting, American Pediatric Surgical Association, New Orleans, La., April 5, 1974.
7. deLorimier, A. A., Tierney, D. F., and Parker, H. R.: Hypoplastic lungs in fetal lambs with surgically produced congenital diaphragmatic hernia. Surgery, *62*:12, 1967.
8. Dibbins, A. W., and Wiener, E. S.: Mortality from neonatal diaphragmatic hernia. J. Ped. Surg., *9*:653, 1974.
9. Holcomb, G. W., Jr.: A new technique for repair of congenital diaphragmatic hernia with absence of the left hemidiaphragm. Surgery, *51*:534, 1962.
10. Kenigsberg, K., and Gwinn, J. L.: The retained sac in repair of posterolateral diaphragmatic hernia in the newborn. Surgery, *57*:894, 1965.
11. Kiesewetter, W. B., Gutierrez, I. Z., and Sieber, W. K.: Diaphragmatic hernia in infants under one year of age. Arch. Surg., *83*:561, 1961.
12. Liebow, A. A., and Miller, H. C.: Congenital defects in the diaphragm. Am. J. Path., *16*:707, 1940.
13. Monclair, T., and Schistad, G.: Congenital pulmonary cysts versus a differential diagnosis in the newborn: Diaphragmatic hernia. J. Ped. Surg., *9*:417, 1974.
14. Moore, T. C., Battersby, J. S., Roggenkamp, M. W., and Campbell, J. A.: Congenital posterolateral diaphragmatic hernia in the newborn. Surg. Gynec. Obstet., *104*:675, 1957.
15. Potter, E. L.: Pathology of the Fetus and Infant, 2nd ed. Chicago, Year Book Medical Publishers, Inc., 1961, pp. 301–302.
16. Riker, W. L.: Congenital diaphragmatic hernia. Arch. Surg., *69*:291, 1954.
17. Roe, B. B., and Stephens, H. B.: Congenital diaphragmatic hernia and hypoplastic lung. J. Thorac. Surg., *32*:279, 1956.
18. Rowe, M. I., and Uribe, F. L.: Diaphragmatic hernia in the newborn infant: Blood gas and pH considerations. Surgery, *70*:758, 1971.
19. Simpson, J. S.: Ventral Silon pouch: Method of repairing congenital diaphragmatic hernias in neonates without increasing intra-abdominal pressure. Surgery, *66*:798, 1969.
20. Simpson, J. S., and Gossage, J. D.: Use of abdominal wall muscle flap in repair of large congenital diaphragmatic hernia. J. Ped. Surg., *6*:42, 1971.
21. Snyder, W. H., and Greaney, E. M.: Congenital diaphragmatic hernia: 77 consecutive cases. Ped. Surg., *57*:576, 1965.
22. Wells, L. J.: Development of the human diaphragm and pleural sacs. Contrib. Embryol., *35*:107, 1954.
23. White, J. J., and Suzuki, H.: Hernia through the foramen of Bochdalek: A misnomer. J. Ped. Surg., *7*:60, 1972.
24. Woolley, M. M.: Postpartum appearance of congenital left posterolateral diaphragmatic hernia. In press.

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Small Bowel Obstructions in the Newborn

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Early diagnosis of newborn intestinal obstruction is important, because if undiagnosed the infant is in great danger of vomiting, particularly if fed, with aspiration and its sequelae. These babies present a challenge to the surgeon because most are salvageable with the proper surgical correction and care.

Congenital gastric obstruction is very rare except for membranous obstruction or atresia occurring at the pylorus or prepyloric area. Malposition and duplications of the stomach do occur but seldom produce a problem in the newborn. In contradistinction, the duodenum is a very common site of congenital obstruction due to embryologic malformations or failure of normal rotation and fixation of the duodenum. There can also be associated constricting extrinsic bands.

DUODENAL OBSTRUCTIONS

The possibility of a duodenal or other high intestinal obstruction should be suspected by the obstetrician if polyhydramnios is found in the mother.[1] Any high intestinal obstruction will prevent the passage of the normally swallowed amniotic fluid; hence the fluid cannot be absorbed in the lower intestinal tract and returned to the mother. It would aid early diagnosis if all infants born of mothers with polyhydramnios were checked for high obstruction. This can be done readily by passing a small nasogastric catheter and aspirating the stomach contents. If there is more than 30 ml of retained secretions or swallowed amniotic fluid, the infant should be further studied. After the stomach is emptied, 30 ml. or more of air is injected and after a short interval, flat and upright x-rays are taken. These films will show dilatation of the proximal duodenum above the site of obstruction. If the obstruction is complete and has been present during a prolonged in utero period, x-rays frequently show the characteristic "double bubble sign" of an enlarged proximal duodenum and stomach frequently with two distinct fluid

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Figure 1. Complete obstruction of duodenum with "double bubble" sign and fluid levels seen in upright roentgenogram.

levels (Fig. 1). The presence of yellow or green bile in the gastric aspirant suggests the possibility of obstruction distal to the ampulla, but it must be remembered that obstructions, atresias, and membranes can occur proximal to the ampulla of Vater, so that gastric contents, or later the vomitus, may not be bile-stained. This absence of bile may lead to delay in diagnosis. It must also be remembered that duodenal obstructions occur in the presence of a scaphoid abdomen. If there is distension, it is limited to the epigastrium or the left upper quadrant and this, too, may be absent if the infant has vomited recently.

Obstructions of the duodenum can occur not only in association with other anomalies of the gastrointestinal tract, but other systems as well. A particularly common association is atresia occurring with esophageal atresia or imperforate anus. Occasionally all three of these anomalies occur in the same patient. Atresia or severe stenosis is frequently found in association with mongoloidism (trisomy 21).

Atresia of the Duodenum

Atresia can occur anywhere along the duodenum but it is most common either proximal to, at, or just distal to the ampulla of Vater. The diagnosis is generally made earlier if the atretic area is distal to the ampulla and the gastric aspirant or vomitus has been bile stained. There will be no intestinal gas pattern distal to the obstruction. The passage of meconium does not rule out intestinal obstruction since debris formed in the lumen of the gut, even distal to an obstruction, may be passed after birth and recorded as a meconium stool.

From a surgical point of view it is helpful that the area of atresia is usually quite short and the proximal dilated bowel tends to be redundant and overhangs the distal small, thinner undistended segment. This frequently allows a duodenoduodenostomy (duodenoplasty) to be done (Fig. 2). A longitudinal incision is made in the long axis of the bowel equally distant from the bowel's medial and lateral attachments and extending roughly the same distance proximally and distally (Fig. 2*a*). It is helpful

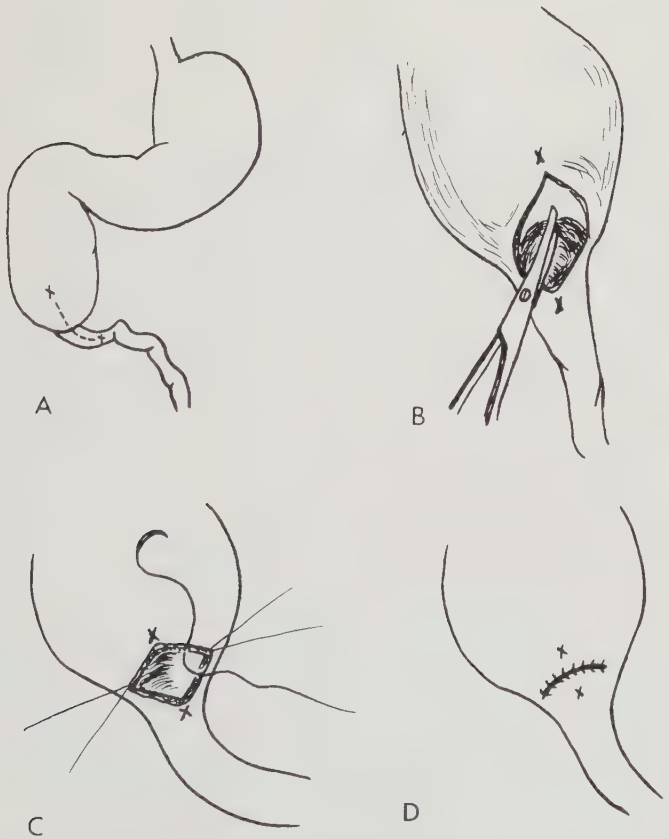

Figure 2. Duodenoduodenostomy. *A*, Longitudinal incision extending both proximal and distal to the obstruction. *B*, Excision of associated intraluminal membrane if present. *C*, Horizontal closure of the longitudinal incision with running catgut suture. *D*, Completed horizontal closure with second layer of interrupted nonabsorbable silk.

to place a marking seromuscular suture approximating the proximal and distal segments at the lateral and medial limits of the eventual repair. Once the longitudinal incisions are made, visualization of the area is easier by holding up these marking sutures (Fig. 2*c*). Care is taken to avoid trauma to the adjacent pancreas. A 5–0 chromic (swedged) suture is then started from either side and with a locking full thickness running suture the duodenal wall is approximated top to bottom producing a horizontal closure (Fig. 2*c*). A second row of interrupted simple 5–0 nonabsorbable sutures* is placed and tied to complete the repair (Fig. 2*d*). This suture must be swedged on a very fine needle in order to avoid trauma to the very delicate seromuscular layer of the distal segment.

Very often a gastrostomy is helpful in decompressing the stomach and the proximal duodenum until this anastomosis begins to function. Frequently edema of the anastomosis prevents adequate emptying for a period of 4 or more days. The presence of a gastrostomy tube eliminates the need for nasogastric suction tube which so often produces pharyngeal secretions and irritation and may set the stage for respiratory problems, especially in the premature. Intraluminal stents or plastic catheters through the anastomosis are not used and seem unnecessary if a wide open anastomosis is achieved. Such a foreign body crossing an anastomosis may lead to perforation and present an unnecessary additional hazard.

Before the gastrostomy tube is placed, a large straight catheter can be passed through the gastrotomy, down through the newly formed duodenal anastomosis to be sure of its size and patency. A number 14 or 16 Malecot catheter is then placed in the stomach and two concentric nonabsorbable silk sutures are placed around the tube to hold the catheter flange inside the stomach to prevent leaking. Two or three extra seromuscular sutures are used to approximate the stomach wall to the parietal peritoneum as the tube makes its exit out through a separate stab wound. It is most important to fix the gastrostomy tube to the skin on either side in order to prevent inadvertent removal of the tube postoperatively. Special attention should be given to the application of adhesive strapping from the tube to the skin in order to maintain the tube's position. If perchance the gastrostomy tube is inadvertently removed early during the postoperative period, a formal surgical procedure is necessary to insure that it has been adequately replaced and that the stomach is adequately secured to the abdominal wall.

The after care of these infants with a duodenoplasty requires patience. Because of the large size and thickness of the proximal duodenum, the duodenum may not empty well even in the presence of a patent, edema-free anastomosis. Since the pylorus remains widely dilated, it is easier for the duodenal secretions to back up and drain out through the nasogastric or gastrostomy tube rather than to pass through the anastomosis into that distal bowel. After an appropriate period of time, usually less than 1 week, the gastrostomy tube, attached to an

*Ethicon 5–0 surgical silk, black braided, Type B, double-armed; half-circle taper, RB-1 needle (Special Order D-1849).

open reservoir, can be elevated and the baby placed in a semi-sitting position to encourage emptying through the anastomosis by gravity. When the gastric drainage diminishes or disappears, trial feedings can be given. It is wise to add through the gastrostomy tube a small amount of 5 per cent glucose in water (15 to 20 ml.). This can be re-aspirated 2 or 3 hours later and an additional amount added to bring the gastric content up to its original volume. It is very dangerous to assume, without this trial of monitored feeding, that all is well and feed by mouth. After successful feeding of glucose water through the gastrostomy, formula feeding should start with a non-curding formula such as Nutramigen. The gastrostomy tube is left open, draining if necessary into the elevated reservoir until the infant is taking a good volume of formula by mouth and the stomach is emptying rapidly. The gastrostomy at this point can be clamped and left in position. It is not removed until 3 to 4 weeks following the surgery to insure adequate union of the stomach to the abdominal wall. Once the gastrostomy tube is pulled, the fistula will close spontaneously and not require a surgical closure. The removal of the gastrostomy tube is usually done in the office when the infant returns for a follow-up visit.

Annular Pancreas

Annular pancreas can be present without symptoms and produce difficulty only in later years due to a constriction of the annulus, probably caused by a mild pancreatitis. In the newborn, however, frequently there is a developmental stenosis or atresia of the duodenum directly beneath the annulus. The symptoms are the same as those produced by a simple atresia or stenosis unassociated with an encircling pancreas. Only the surgeon at the time of exploration can determine whether the atresia or stenosis is indeed associated with abnormal encirlement by the pancreas.

To correct a stenosis or atresia beneath an annular pancreas, it is dangerous to transect the annulus itself, which can lead to a leak of pancreatic juice or the interruption of a major duct. Therefore, primary duodenoplasty is unwise; a by-passing duodenojejunostomy should be performed, leaving undisturbed the encircling ring of pancreas (Fig. 3). It is important that this end-to-side anastomosis be done so there is adequate drainage from the afferent limb into the duodenum and from the duodenum into the efferent jejunum limb. This anastomosis is performed retrocolically, bringing the proximal, dilated duodenum through a hole made in the transverse mesocolon. The most distal dependent portion of this duodenum is opened transversely but only after the posterior row of nonabsorbable silk sutures has been placed. This posterior row should be placed close to the jejunum mesentery so that there is ample bowel for suturing the anterior seromuscular layer when the anastomosis is being completed. It is helpful before the small jejunal segment is opened, parallel to this posterior row of sutures, to inject saline into the lumen of the bowel which will distend it and make the subsequent completion of the anastomosis easier (Fig. 3*b*). Once both segments are opened for the full extent of the proposed anastomosis, a

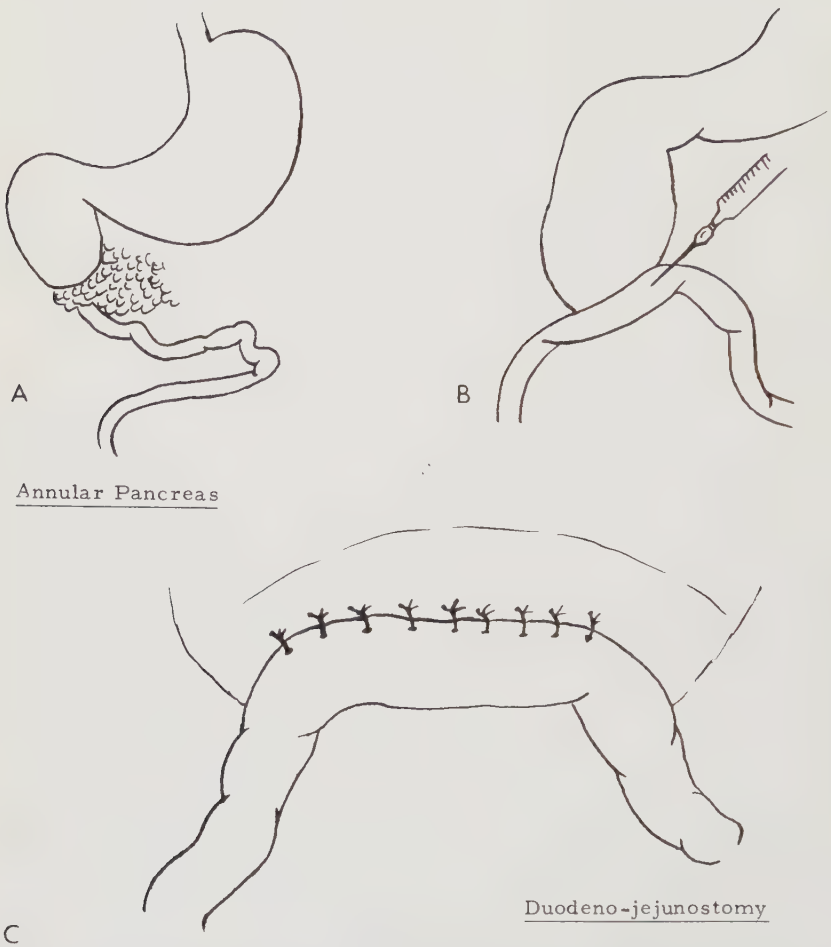

Figure 3. *A*, Annular pancreas encircling duodenum with atresia or stenosis beneath the annulus. *B*, Injection of saline into jejunal limb which dilates and allows for a safer anastomosis. *C*, Completed end-to-side duodenojejunostomy lying comfortably along the under aspect of transverse mesocolon.

no. 5 chromic catgut (swedged) suture is then started in the middle of the posterior layer and with full-thickness bites of both duodenum and jejunum, it is carried around as a running suture to the anterior midportion of the anastomosis. A second similar suture is placed going around the other side of the anastomosis. Before the anterior closure is complete, it is helpful to place a catheter through the anastomosis and into one of the jejunal limbs. At this point several seromuscular sutures are placed and tied. The same procedure is used on the opposite side guaranteeing that none of the sutures are placed too deeply and that the lumen will be as widely open as possible. Once the catheter has been removed the remaining portion of the anastomosis can be closed with catgut followed by the remaining interrupted seromuscular sutures of silk (Fig. 3*c*).

The edges of the transverse mesocolon through which the duodenum emerges are then approximated to the duodenum just above the anastomosis which allows the loop of anastomosed jejunum to lie comfortably in a gentle arc along the underside of the transverse mesocolon (see Fig. 3*c*). Special care should be taken that both the afferent and efferent limbs are not kinked or twisted. A gastrostomy decompression of the stomach should always be used since a duodenjejunostomy may be slow to function.

The postoperative care must be carefully followed. Only after the gastrostomy drainage diminishes should feedings be started as previously described. Known amounts of glucose water are added through the gastrostomy and the residual checked before adding a second feeding. After proving that the anastomosis is emptying well, Nutramigen can be carefully started and the amounts of the feedings increased.

Duodenal Membranes

Membranous obstruction of the duodenum is less common and can be found anywhere from the pylorus to the ligament of Treitz, but occurs most frequently in the descending portion of the duodenum close to the ampulla. Such membranes may be imperforate or may have a small hole through which intestinal content flows with difficulty. If imperforate, the symptoms and x-ray appearance are similar to those produced by atresia. If a small perforation is present, some gas may pass into the distal bowel but since the perforation is small, the infant is in trouble at or soon after birth.

Although most of these membranes stretch tightly across the lumen of the duodenum, an occasional one is thin and balloons distally producing a "wind sock" deformity. The membrane distends downward into the distal bowel but its annular site of attachment remains more proximal.

The surgical excision of membranous obstruction is done by opening the duodenum longitudinally above and below the membrane, the same approach as is used for atresia (see Fig. 2*a*). The membrane is then excised and the mucosal edge is oversewn with a fine hemostatic suture (see Fig. 2*b*). This same suture then continues around, picking up with full-thickness bites, the previously made longitudinal incision

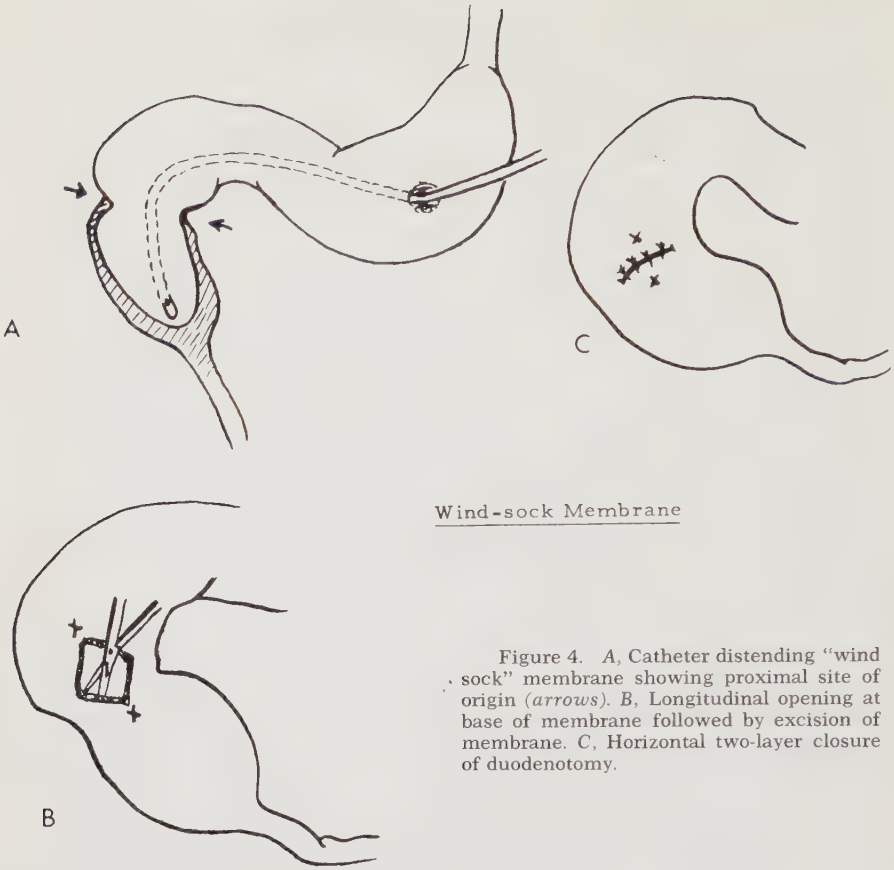

Figure 4. *A*, Catheter distending "wind sock" membrane showing proximal site of origin (*arrows*). *B*, Longitudinal opening at base of membrane followed by excision of membrane. *C*, Horizontal two-layer closure of duodenotomy.

closing them in a horizontal direction (see Fig. 2*c*). A second row of interrupted silk seromuscular sutures is placed and tied (Fig. 2*d*). The lumen is, therefore, enlarged by both the excision of the membrane and by the method used to close the bowel. Special attention should be taken if a membrane occurs adjacent to, or actually involves the ampulla of Vater. In order to avoid trauma to the common bile duct or inadvertent closure of the ampullary opening, it may be necessary to leave a portion of the membrane undisturbed.

A membrane that has produced a "wind sock" deformity requires a special approach. Since the membrane distends the duodenum distal to its attachment, its point of origin may not be apparent. The duodenum, therefore, should not be opened at the point where the bowel becomes smaller in calibre since this would be at the apex of the membrane rather than at its base. To avoid this error, a fairly firm rubber catheter or flexible small Bockus dilator should be inserted through a gastrotomy and passed down through the pylorus (Fig. 4*a*). This catheter or dilator will stretch the elongated membrane and show the attachment at a more proximal level. The longitudinal opening of the duodenum should

be performed at this proximal site and the entire redundant membrane can be excised and the repair and closure accomplished as described above (Fig. 4,*b* and *c*). A gastrostomy tube is then placed in the gastrotomy hole and sutured and exteriorized in the standard fashion.

The postoperative care is similar to that described for atresia; however, with the larger lumen obtained, earlier feeding may be possible.

Duodenal Bands Without Malrotation

Occasionally extrinsic bands can form across the duodenum producing obstruction or narrowing the duodenal lumen by extrinsic pressure. These bands produce the same symptoms of complete or incomplete obstruction mentioned above and their presence, as a cause of obstruction, cannot be determined prior to surgery.

These adventitial bands can be transected without damaging the duodenal wall. It is most important, however, to rule out a concurrent internal obstruction. Gastrotomy should be performed and the calibre of the duodenum checked by a catheter or flexible dilator (Fig. 5). If an associated intraluminal obstruction is found, it should be repaired.

Duodenal Bands With Malrotation

The signs of intestinal obstruction in the newborn may be due to extrinsic bands across the duodenum occurring with malrotation of the intestinal tract and abnormal posterior fixation. In such cases, the duodenum and colon fail to complete their normal rotation so that the duodenojejunal junction may be in the midline or even to the right of the midline rather than in the normal position at the ligament of Treitz.

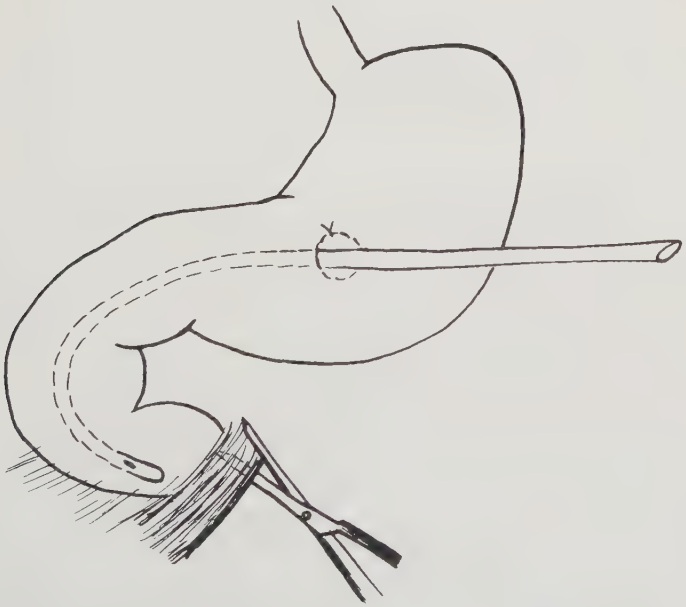

Figure 5. Catheter traversing gastrotomy to prove patency of duodenal lumen beneath extrinsic bands.

Similarly, the ileocecal valve may be in the upper abdomen rather than making its full rotation and ending up in the right lower quadrant. This is a most urgent form of intestinal obstruction since the beginning and end of the small bowel mesentery are close together and there is great danger of a midgut volvulus occurring around the axis of the superior mesenteric artery. When the volvulus occurs after birth, there is venous engorgement and blood may be passed in the stools. As the volvulus becomes tighter, not only is there venous engorgement, but the arteries are compressed with resulting gangrene and loss of the entire midgut from the proximal jejunum down to the terminal ileum or beyond. Such a volvulus can occur in utero prior to birth but frequently occurs after birth. If recognized, surgery can be performed before the bowel becomes necrotic.

Often the proximal duodenum is not as dilated as is seen in duodenal atresia since the extrinsic bands cause incomplete obstruction of the duodenum. With such an incomplete obstruction, barium can be safely given and may pass through the partially blocked duodenum, showing the proximal jejunal loops to be in the right upper quadrant rather than in the left where they normally are found. The barium may also demonstrate an absence of a normal C-shaped duodenum ending at the ligament of Treitz. A barium enema study may show the cecum to lie in the right upper quadrant suggesting failure of full rotation, although this finding may only imply that there is a mobile cecum rather than true malrotation. The x-ray evidence of an existing volvulus is variable. A "corkscrew" appearance of the upper jejunum is occasionally seen if the volvulus has not produced a complete obstruction. There may also be dilatation of jejunal loops if there is outflow obstruction from the twisted segments. It must be concluded that if the x-ray studies suggest the possibility of malrotation with or without definite evidence of an associated volvulus, surgery must be considered immediately before irreversible damage occurs. The possibility of malrotation should be high on the priority list when one is evaluating upper intestinal obstruction in the newborn.

The time-proven method of repair first described by Dr. William E. Ladd[3] is still the procedure of choice. It is essential to deliver as much of the gut through the abdominal wound as possible in order to recognize a possible volvulus and reduce it, usually by turning it in a counterclockwise direction. Once the volvulus is reduced, the bands crossing over the duodenum are lysed along with any other anomalous bands connecting various portions of the intestinal tract one to another. This frees the duodenum. The ascending and transverse colon hangs free on the mesentery. The duodenum can be placed to lie in a fairly straight line just to the right side of the midline; the remaining small bowel is placed in the right half of the abdomen; and the entire colon is placed on the left side, usually with the cecum in the left lower quadrant. No effort is made to establish a normal position for the intestinal tract in the abdominal cavity. The bowel is not sutured to its new location since postoperative adhesions prevent a volvulus from recurring postoperatively. Unfortunately, with the extensive dissection required and considerable

Figure 6. Volvulus with gangrene of entire midgut secondary to malrotation. Inadequate length of viable intestinal tract remains.

raw areas produced by a classical Ladd's procedure, there is a high incidence of postoperative intestinal obstruction due to adhesive bands that may require subsequent laparotomy.

Malrotation with volvulus will be diagnosed and treated only if its presence is suspected. Delay can be catastrophic. If the midgut is gangrenous, there is often insufficient bowel for the future growth and survival of the patient (Fig. 6).

JEJUNAL AND ILEAL OBSTRUCTION

Atresias involving either the jejunum or the ileum ordinarily do not have much distension at birth but become distended rapidly as the newborn swallows air. High jejunal obstruction produces distension primarily of the upper abdomen; obstructions lower down usually lead to more generalized abdominal distension. These infants always vomit bile; they may or may not pass some meconium. An infant with meconium ileus is generally more distended and the distension is present at birth. He usually vomits soon after birth and the vomitus is always bile stained. Frequently the distended small bowel loops can be seen through the intact, thin abdominal wall and peristaltic waves may be observed. Such an infant may have a "putty sign" where the examining finger indents through the abdominal wall the meconium in a dilated loop and the indentation persists due to its semisolid nature.

Figure 7. Intraperitoneal calcifications secondary to meconium peritonitis. Arrow demonstrates calcification in indirect inguinal hernia sac.

Any obstruction beyond the duodenum may be complicated by perforation. If perforation occurs in utero, there can be meconium peritonitis with intraabdominal calcifications visible on an abdominal x-ray film (Fig. 7). Such calcification may be seen in the absence of free air since perforations may seal over or completely close prior to the infant's birth. An infant with meconium peritonitis, however, may be markedly distended at birth; the abdominal wall may have a brownish or reddish appearance suggesting a severe reaction of the parietal peritoneum, apparent through the thin abdominal wall (Fig. 8). Intraabdominal fluid collections may loculate and the bowel may therefore be pushed into one small portion of the abdominal cavity. If such a loculation does not occur, the bowel may be seen on x-ray films to be floating on the excessive fluid in the peritoneal cavity. If there is free air, the presence of a persisting perforation is obvious. Occasionally a perforation seals and the bowel lumen remains in continuity; evidence of an old in utero peritonitis may be only an incidental finding. Exploration is done only if there is evidence of obstruction or a leak.

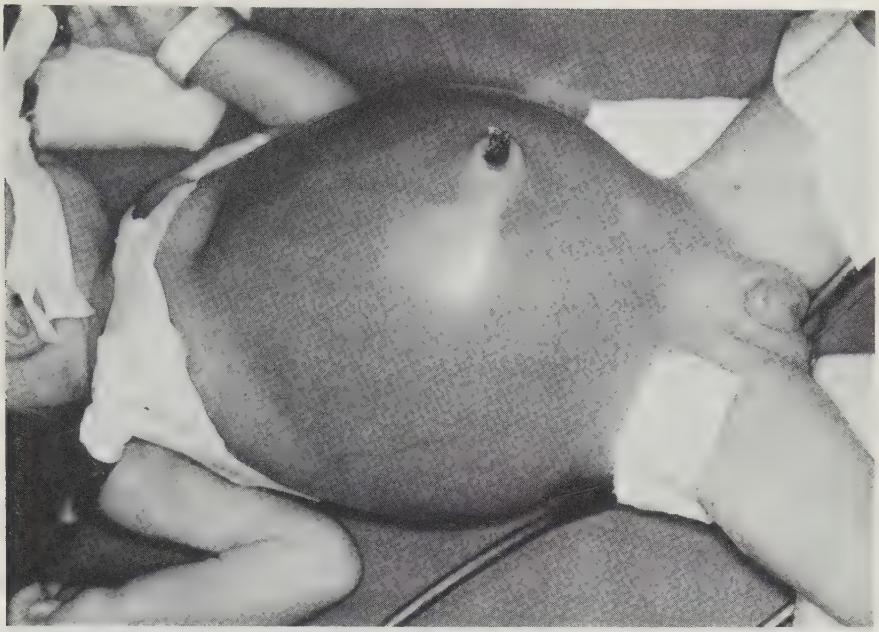

Figure 8. Distended, discolored abdominal wall secondary to long standing in utero meconium peritonitis.

Jejunal and Ileal Atresia

In the past these obstructions were thought to be congenital abnormalities, embryologic malformations of the gut. Louw and Barnard[5] demonstrated beautifully that atresia can be acquired due to a compromise of the intestinal vasculature secondary to an unexplained intraabdominal catastrophe occurring after the fetal bowel was normally formed. They produced atresia in fetal pups by ligating segments of the bowel or segments of the mesentery, replacing the fetus back into the uterus for further growth. Later it was found that atresias were produced which were typical of those seen in the human newborn. A simple ligature placed around the fetal bowel would produce an area of atresia that was immediately adjacent to the collapsed bowel distally. If a major arterial supply was interrupted, atresia was produced with a gap between the proximal and distal segments and an absence of a segment of mesentery. It is interesting that those intervening segments of gangrenous bowel can be absorbed completely and leave no remnants. Ligating a loop of bowel similarly leads to a disappearance of that loop with a resultant acquired atresia. Their work completely altered our concept of the origin of atresia in humans; many undoubtedly are due to an intraabdominal vascular catastrophe occurring in the human fetus after the bowel is normally formed. The presence of squamous cells and lanugo hair may therefore be found in the meconium distal to such an acquired in utero atresia, making that finding unreliable to rule out the presence of bowel atresia.

Characteristically, abdominal x-rays show dilated loops of small

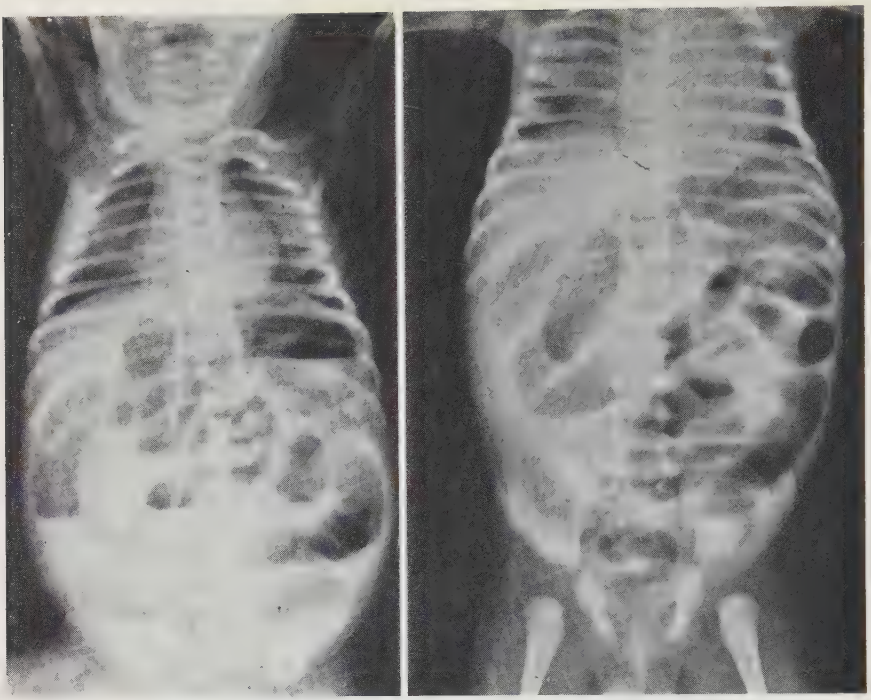

Figure 9. Roentgenograms of newborn with ileal atresia. Multiple fluid levels are seen in the upright film (*left*). Multiple dilated loops of similar size are seen in supine film (*right*).

bowel which are generally of the same calibre and fluid levels can be seen in the upright films (Fig. 9).

Early pediatric surgeons felt that exteriorization by Mikulicz double barrel enterostomy was the safest way of staging the repair of small bowel obstructions. Currently most surgeons prefer primary anastomosis whenever possible, even in the presence of perforation and meconium peritonitis. Such meconium peritonitis may be merely a chemical, not bacterial, peritonitis and does not require an exteriorization procedure that might be used with the presence of a bacterially contaminated peritonitis.

There is characteristically bulbous distension of the bowel proximal to an atresia extending proximally for 10 cm or more. This segment if left in the circuit functions poorly. If the bowel is of adequate length, it is wise to resect the dilated seegment before anastomosing the segments together (Fig. 10*a*). It is helpful to distend the distal unused bowel by injecting saline into it. This not only distends it to allow for an easier anastomosis, but it is possible to follow the saline down to the ileocecal valve, hence proving the absence of any other unsuspected atresias (Fig. 10*b*). Most pediatric surgeons feel that demonstrable patency only to the ileocecal valve is sufficient; the colon is assumed to be patent unless it appears grossly abnormal. If there is doubt about the patency of the colon, it can be distended by injecting saline through a previously placed rectal tube from outside the sterile field. After resec-

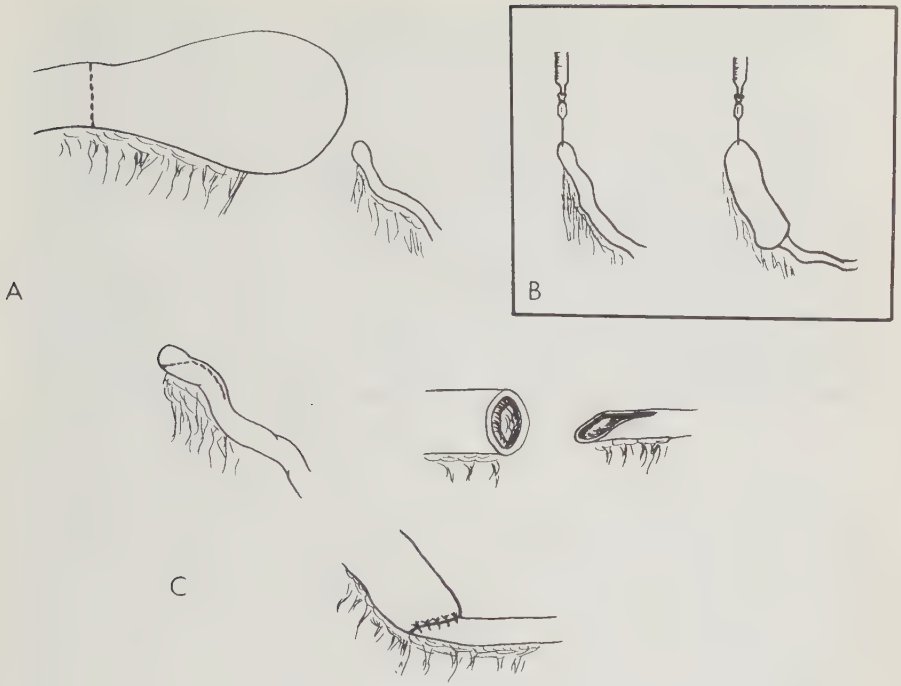

Figure 10. *A*, Jejunal or ileal atresia with bulbous distention of proximal end showing site of resection. *B*, Saline distension of distal collapsed bowel demonstrating an otherwise unrecognized second area of atresia. *C*, Oblique opening of antimesenteric border of distal bowel showing end-to-back anastomosis using a two-layer technique.

tion of the proximal dilated segment, the transverse end of the bowel can be anastomosed obliquely to the antimesenteric side of the distal bowel using a two-layer technique (Fig. 10c). The interrupted seromuscular sutures are of 5–0 interrupted silk and a running locking 5–0 chromic suture is used for the full-thickness approximation of the inner layers. Again it is wise to check the patency of the final anastomosis before the catgut sutures meet anteriorly as was previously described. A catheter can be passed through the most critical part of the anastomosis where the anastomosis empties into the small lumen of the distal bowel. With the catheter in place the interrupted silk sutures of the second layer can be placed and tied to guarantee that the lumen is adequate. After the catheter is removed the running first layer catgut closure is completed and this is followed by the remaining interrupted silk sutures of the second layer. In this way the anastomosis can be completed with confidence that the anastomosis is open and should function early.

The mesenteric rent should be approximated but care is taken not to ligate or tear the mesenteric vessels. This is safely done by placing a mosquito hemostat on the peritoneum on each side of the defect and approximating these by a simple ligature rather than running the risk of passing a needle through the mesentery and damaging an important vessel.

Side-to-side anastomosis, although technically easier, should not be done since the peristaltic stream enlarges the proximal blind end and may produce a "blind end syndrome" with poor functioning of the anastomosis and the possibility of abnormal bacterial growth occurring in the blind sac. Turning the distal segment back on the proximal segment producing antiperistaltic side-to-side anastomosis is equally dangerous and will produce a poorly or nonfunctioning anastomosis. The "end-to-back" (oblique) anastomosis described above has proven very successful and is now used routinely.

These small bowel anastomoses for atresia generally open up and function early, hence gastrostomy decompression is not used, except perhaps in the premature infant where an indwelling nasogastric tube may be dangerous. Since the bowel can decompress back through the relaxed pylorus, gastric suction alone is effective in keeping the bowel free of excessive distension until the ileus disappears. Gastric suction is, of course, important until the anastomosis begins to function. The nasogastric tube should be irrigated frequently to insure adequate drainage. Intraluminal stents are not used but care is taken when placing the anastomosed segments back in the abdomen to have them lie in a gentle arc, avoiding any kinking or twisting, especially the thin distal collapsed segment.

Meconium Ileus

Five to 10 per cent of infants born with fibrocystic disease of the pancreas will have small bowel obstruction due to abnormal inspissated meconium resulting from inadequate secretions of enzymes from the pancreas and the bowel mucosa. Frequently there is a family history of the disease. Unfortunately, after the obstruction is relieved, these youngsters are prone to have pulmonary and other problems because of abnormal bronchial secretions. Since the lung complications are so serious, it is well to avoid the risk of anesthesia and surgery, if possible. Dr. Helen Noblett[6] deserves credit for describing the use of fluoroscopically controlled gastrografin enemas as a nonsurgical method of relieving the intraluminal obstruction. Gastrografin (meglumine diatrizoate) contains a wetting agent, Tween-80 (polyoxyethylene sorbitan mono-oleate). When used as an enema, it is capable of separating the very viscid, tenacious meconium from the mucosal wall. Gastrografin has a high osmolarity (1900 mOsm per L), thus fluid is pulled into the intestinal tract, which further aids in the evacuation of the abnormal meconium. Great patience and skill are required when using this nonsurgical method. All these infants should have adequate gastric decompression with a well functioning nasogastric tube and intravenous replacement should be in process during the time of the enema and afterwards to make up for the excessive fluid losses into the intestinal tract. The fluoroscopist watches the gastrografin gradually flow through the small colon. Hopefully it will then surround the small pellets that fill the terminal ileum and will eventually be refluxed into the large dilated segments which are packed with the putty-like meconium (Fig. 11). A single gastrografin enema may be adequate, but frequently a second or third enema must be given at intervals of 4 to 8 hours.

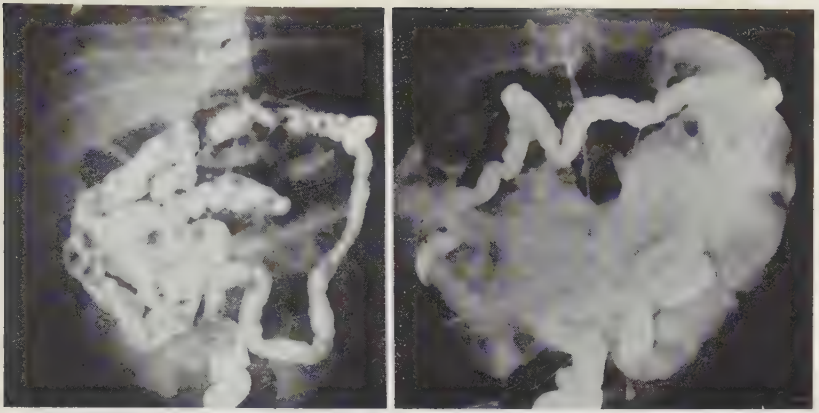

Figure 11. Gastrografin enema outlining small, unused colon and inspissated pellets in terminal ileum *(left)*. Continued reflux of gastrografin into dilated small bowel loops containing inspissated meconium *(right)*.

In order to use this nonsurgical method, it is of course essential that the preoperative x-ray diagnosis be accurate. The roentgen findings are fortunately quite characteristic (Fig. 12). There is a great disparity in the size of the various loops and a scarcity or absence of fluid levels in the upright film since the tenacious meconium will not layer as it does with a more liquid bowel content seen in other forms of intestinal ob-

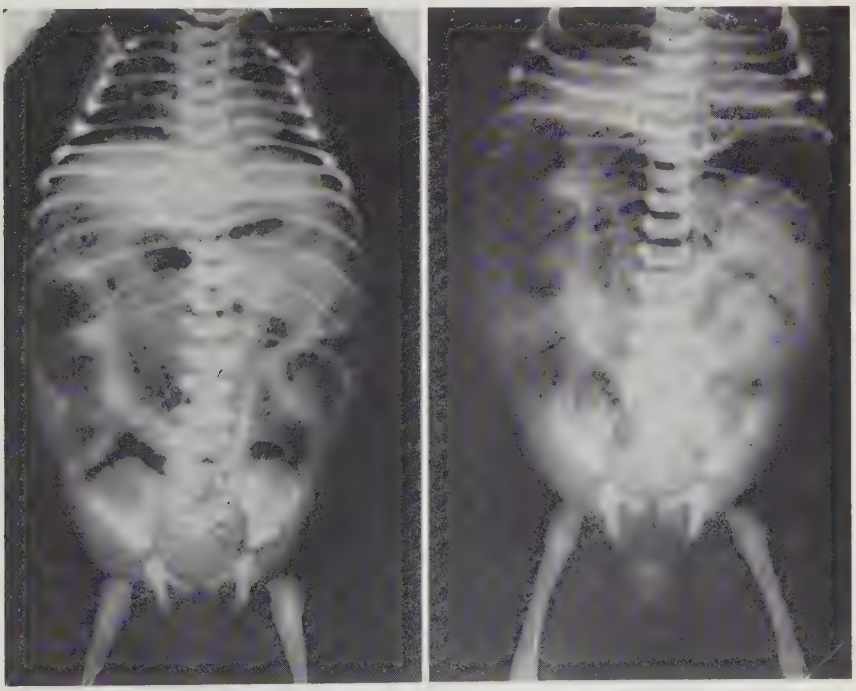

Figure 12. Classical roentgenogram of meconium ileus showing dilated loops of variable size, "soap bubbling," and the absence of fluid levels in upright film *(right)*.

struction. There is frequently a "soap bubbling" or "ground glass" appearance caused by the air coming down the small bowel and forcing air bubbles into the thick meconium. The classical gastrografin enema findings of course further substantiate the presence of this relatively unusual condition.

Roughly 50 per cent of infants cannot be relieved by gastrografin enemas alone and the problem must be dealt with surgically in spite of associated risks. A volvulus of the maximally dilated loop of ileum, frequently with an associated atresia, requires surgery. An in utero perforation as shown by intraperitoneal calcification or the presence of free air requires immediate surgery.

Many operative approaches have been used. Gross[2] improved survival rates greatly by using a Mikulicz double-barrelled ileostomy with postoperative irrigation of pancreatic enzymes into the distal bowel. Unfortunately this method requires an early closure of the leaking ileostomy after the common wall has been crushed. This second surgical procedure frequently leads to further pulmonary complications. In 1959 Bishop and Koop[1] described a modification of the exteriorization technique (Fig. 13). The maximally dilated loop is resected and by a roux-en-Y anastomosis a single limb ileostomy is constructed and exteriorized through a separate incision. With the abdominal incision still open, a catheter is threaded down into the distal limb, down past the end-to-side anastomosis (but not through it), and into the obstructing meconium. The abdominal wall closure is simplified since the massively dilated segment is resected, and at the end of the procedure the intestinal tract is open from mouth to ileostomy. Postoperatively pancreatic enzymes (Viokase) can be irrigated through the catheter which gradually liquefies the meconium; it is passed at first in a retrograde fashion back and out through the ileostomy, and finally distally in the lower ileum and colon. After the distal obstruction is relieved the peristaltic stream is all downward and the infant is left with a nonfunctioning mucous fistula. This ileostomy can be trimmed down to skin level by applying a crushing heavy ligature or by cutting it off with a coagulating current. Many will close gradually, thereby avoiding the necessity of a subsequent anesthesia and surgical closure. If a repair is needed, it can be done at a much later time when the child is hopefully better able to withstand the risk of another anesthetic. This roux-en-Y exteriorization method has been used even in the presence of complications of disease. A twisted loop can be resected or an atretic end can be resected and the end of the proximal segment anastomosed in the usual fashion to the side of the distal, still obstructed bowel. The roux-en-Y procedure seems safe even in the presence of a chemical peritonitis related to an in utero perforation.

All of these infants once relieved of their intestinal obstruction, either by enema or surgery and postoperative irrigations, will subsequently need experienced medical care to minimize the complications of their generalized disease which involves all of the exocrine glands of the body. Pancreatic extracts must be given with feedings to aid intestinal absorption. Chest physiotherapy, extra humidity, and judicious use of antibiotics is important to minimize the life-threatening pulmonary

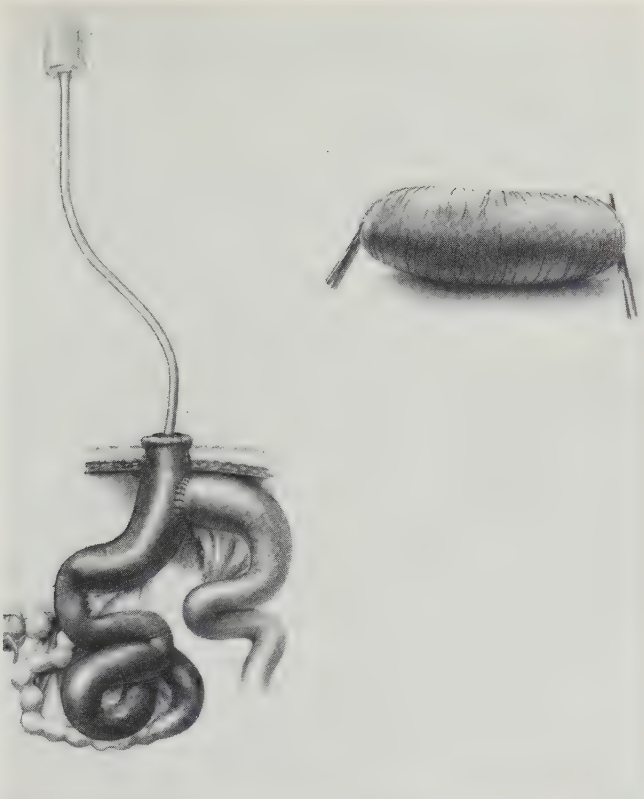

Figure 13. Resection of dilated ileal loop with end-to-side Roux-en-Y anastomosis and single limb ileostomy. Catheter enters the distal bowel for later irrigation with pancreatic enzymes.

complications. Many specialized centers are now organized for the complicated care of these children.

Segmental Volvulus

Occasionally an infant with intestinal obstruction is found to have a short segment of bowel twisted upon itself for no apparent reason, unrelated to any abnormal fixation or abnormally retained meconium. If such a loop is found it can be resected and a primary "end-to-back" anastomosis can be used to re-establish bowel continuity. If there is a question about distal obstruction due to inspissated meconium sometimes seen even in the absence of pancreatic insufficiency, a Roux-en-Y type of exteriorization can be done similar to the procedure used for meconium ileus.

CONCLUSION

With current knowledge and skill, any infant with duodenal, jejunal, or ileal obstruction should be diagnosed soon after birth. In the absence

of other congenital defects or complications, surgical correction should be successful in the vast majority of cases. These infants, with the exception of those with meconium ileus, can be expected to have a normal life span.

REFERENCES

1. Bishop, H. C., and Koop, C. E.: Management of meconium ileus: resection, roux-en-Y anastomosis and ileostomy irrigation with pancreatic enzymes. Ann. Surg., *145*:410, 1957.
2. Gross, R. E.: The Surgery of Infancy and Childhood. Philadelphia, W. B. Saunders Co., 1953, p. 183.
3. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood. Philadelphia, W. B. Saunders Co., 1941, p. 63.
4. Lloyd, J. R., and Clatworthy, H. W., Jr.: Hydramnios as an aid to the early diagnosis of congenital obstruction of the alimentary tract: a study of the maternal and fetal factors. Pediatrics, *21*:903, 1958.
5. Louw, J. H., and Barnard, C. N.: Congenital intestinal atresia: observations on its origin. Lancet, 2:1065, 1955.
6. Noblett, H. R.: Treatment of uncomplicated meconium ileus by gastrografin enema: a preliminary report. J. Ped. Surg., *4*:190, 1969.

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Hirschsprung's Disease

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Hirschsprung's disease is a congenital anomaly which can range in severity from complete intestinal obstruction in the newborn period to varying degrees of constipation from birth onward. It is caused by an absence of the ganglion cells of the pelvic parasympathetic system in both Auerbach's plexus between the circular and longitudinal muscle layers of the colon and Meissner's plexus in the submucosa.

The disease was first described in 1888 by Hirschsprung,[10] who found in the autopsies of two children the massive dilatation and hypertrophy of the colon and considered this the site of the disease.

In 1908 Finney[8] described nine theories concerning the etiology of the disease, among which he postulated a "neuropathic dilatation" of a portion of the colon as a possible etiology. He also described ganglion cells in the myenteric plexus of the hypertrophied segment but did not study the distal narrowed segment. Dalla Valle[5] in 1920 was the first to describe the distal contracted segment of bowel as an area in which there were absent ganglion cells. Further observations on the aganglionic segment were made by Cameron in 1928,[4] Robertson and Kernohand in 1938,[15] and Tiffin, Chandler, and Faber[27] in 1940.

As a result of these findings, it was thought during the 1940's that obstruction was caused by an uninhibited sympathetic system and so sympathectomy was suggested as a means to balance the impaired parasympathetic innervation. Drugs such as Mecholyl to stimulate peristalsis were also tried. These methods met with little success. In 1948 Swenson and Bill[24] reported the first successful operation for correction of Hirschsprung's disease by focusing on the removal of the aganglionic segment with preservation of the internal anal sphincter.

The etiology of Hirschsprung's disease is not known, but the work of Okamoto and Ueda[13] may indicate the pathogenesis. In a study of 18 human fetuses they found that the myenteric plexus is first formed by neuroblasts which progress along the alimentary tract in a craniocaudal manner during the fifth to twelfth week of gestation. Aganglionosis may result if there is a cessation of the migration of these cells and the length of the segment varies according to the time of the arrest. Al-

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though the ganglion cells fail to descend, the preganglionic parasympathetic fibers that would have joined these cells continue to elongate and become hypertrophied in the aganglionic segment. This was first noted by Bodian[2] who described the fibers as being characteristic of the disease.

The internal anal sphincter is aganglionic in every case of Hirschsprung's disease. Approximately 80 per cent of the cases involve the rectosigmoid and about 15 per cent have aganglionic segments extending as far proximally as the hepatic flexure.[9] Stone[21] reported 55 cases involving the entire colon; in many of these a short ileal segment was involved; and there is one reported case of total aganglionosis. A few cases of aganglionosis involving skip areas have been reported but most pathologists now doubt that there is such a type.

In Hirschsprung's disease there is absence of peristalsis in the aganglionic segment, thus producing intestinal obstruction. Swenson demonstrated this graphically by a classic and simple experiment.[22] He inserted three recording balloons into the left side of the colon of a child who had a transverse colostomy because of Hirschsprung's disease. One balloon was placed at the splenic flexure, a second one in the descending colon, and the third balloon in the rectosigmoid. Recordings taken from each of these sites showed that the upper colon produced normal peristaltic waves progressing downward to the rectosigmoid, but in the aganglionic segment of the rectosigmoid there were only ineffectual and uncoordinated peristaltic contractions.

Manometric studies described by Schuster[16, 17] showed that on stimulation of the rectum by distending with air a series of balloons inserted into the anal canal, there is no relaxation of the internal anal sphincter in Hirschsprung's disease (Fig. 1). In the normal individual, stimulation of the rectum produces a reflex relaxation of the internal anal sphincter (Fig. 2).

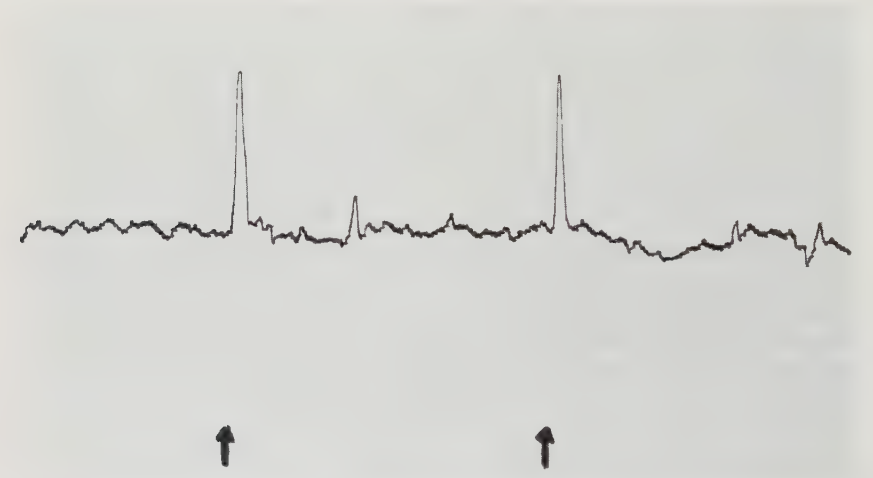

Figure 1. Hirschsprung's disease: Manometric study of internal anal sphincter showing no relaxation.

Figure 2. Normal child: Manometric study of internal anal sphincter showing relaxation.

These studies would indicate that the sphincter and aganglionic segment are in a constant state of tonic contraction, and the pathophysiology of this condition was recently clarified by Ehrenpreis.[7] Using sensitive neurohistochemical techniques, Norberg[12] found that there are normally sympathetic adrenergic fibers connecting with the ganglion cells in the myenteric plexus in addition to the parasympathetic fibers. Heretofore it was believed that only parasympathetic fibers formed networks around the ganglion cells. Using this technique on segments of aganglionic colon, Ehrenpreis found that the terminal networks of sympathetic fibers were absent. This indicates that there is a functional denervation of the aganglionic segment. According to Ehrenpreis it confirms Cannon's law that denervated smooth muscle is abnormally sensitive to stimuli and tends to contract permanently.

Lack of peristalsis in the aganglionic segment and failure of relaxation of the internal anal sphincter produce the varying degrees of intestinal obstruction found in Hirschsprung's disease and explain the configuration of the colon. The bowel proximal to the aganglionic segment becomes gradually dilated and hypertrophied for a variable length as the peristaltic waves try to propel stool into the obstructing aganglionic segment. The visible transition zone between dilated bowel which contains ganglion cells and normal sized bowel which is aganglionic does not coincide exactly with the histologic picture, because constant propulsion of stool against the aganglionic segment will dilate its upper portion slightly, an important factor in the proper placement of a colostomy during the staged treatment of Hirschsprung's disease.

DIAGNOSIS AND MANAGEMENT

In the older child the differential diagnosis is often between chronic or psychogenic constipation and Hirschsprung's disease. In most cases

the diagnosis can be made on the basis of history alone. A child with Hirschsprung's disease is constipated from the first day of life and will always have had problems moving his bowels. The child with chronic constipation usually has problems up until some time in infancy when he may develop a painful fissure which causes withholding of stool. Or there may have been a traumatic period during toilet training, producing psychogenic constipation. The child with Hirschsprung's disease is frequently chronically ill and has a distended abdomen. The child with chronic constipation will pass enormous stools which can block the toilet. There is often fecal incontinence at night and encopresis (soiling of his underpants) during the day. The child with Hirschsprung's disease can never pass a stool of any great size and never has encopresis. This type of soiling cannot occur because the state of tonic contraction of the internal sphincter prevents involuntary leaking of stool around an impaction.

The constipated child, although he retains large amounts of fecal material which are easily palpable, usually has a flat abdomen because gas escapes normally. The abdomen of the child with Hirschsprung's disease is distended with gas, liquid, and inspissated feces. On rectal examination the aganglionic rectum of Hirschsprung's disease is empty and the internal sphincter feels tight. Fecal material does not enter the aganglionic segment because it is contracted and aperistaltic, although over a long period of time the fecal bolus may dilate this segment somewhat by constant pressure. The constipated child, in contrast, has an enormous rectum and frequently there is stool bulging at the anus.

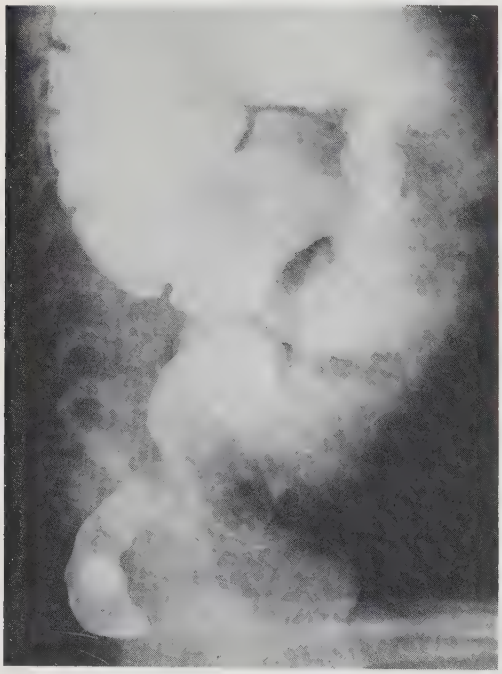

Figure 3. Hirschsprung's disease: Barium showing narrow aganglionic segment of rectosigmoid.

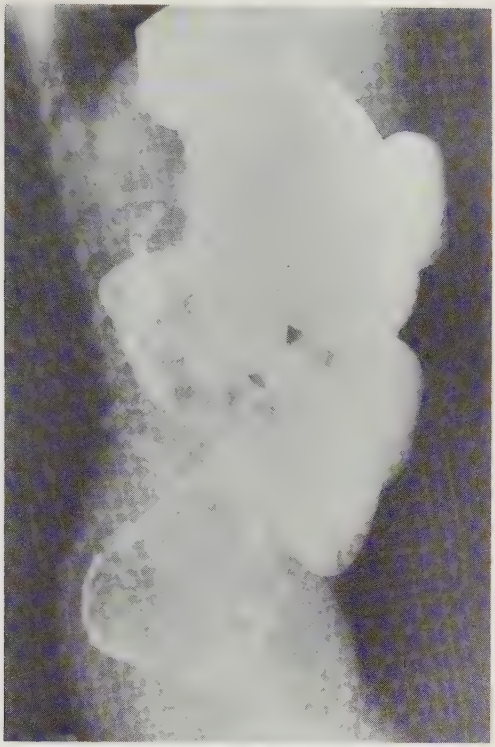

Figure 4. Psychogenic constipation: Barium enema showing large fecal impaction in rectum, no aganglionic segment.

Radiologically a barium enema will demonstrate a narrow aganglionic segment, often with a saw-toothed outline (Fig. 3). This can be difficult to show if the child has a very short segment involved or if the entire colon is aganglionic. In the child with chronic constipation the barium extends into the greatly dilated rectal ampulla or there may be a huge fecal impaction situated at the anal verge (Fig. 4). Cleansing enemas prior to these studies should not be given because the characteristic configuration of the bowel will be lost if the colon is evacuated.

Manometric studies can be done easily in the older child and the absence of relaxation of the internal anal sphincter will confirm the diagnosis of Hirschsprung's disease.

Rectal biopsy is seldom necessary to make the diagnosis if manometric examination is available, but an intraabdominal biopsy can be done to confirm the diagnosis at the time of colostomy or pullthrough procedure.

In the newborn with Hirschsprung's disease, the diagnosis can often be difficult. The infant may present with bizarre symptoms of obstruction or constipation followed by explosive diarrhea-like stools. There is often abdominal distention and vomiting, yet the baby may at times appear perfectly normal.

Ninety per cent of 323 newborns in Swenson's[26] most recent series of 501 patients presented with a varying combination of these symptoms. Failure to pass meconium within the first 24 hours of life should

suggest Hirschsprung's disease if other causes of mechanical obstruction have been ruled out. Occasionally perforation of the cecum may be the first sign of this anomaly.

In some babies the symptoms may suggest mild gastroenteritis or a feeding problem associated with mild constipation. As the condition becomes more chronic the baby fails to gain weight, becomes hypoproteinemic and edematous, and suffers with intermittent episodes of severe constipation and diarrhea. Eventually enterocolitis may develop, an often lethal complication of Hirschsprung's disease. The clinical picture includes fever, vomiting, watery or bloody diarrhea, hypovolemia, septic shock, and finally death.

The etiology of enterocolitis is not known. Swenson[22] believes that there is impaired immunity in these infants with a possible defect in water metabolism and electrolyte control. Stasis of fecal material in the dilated and obstructed colon may produce erosion and ulceration of the mucosa. Because of extremely high concentrations of organisms in the obstructed bowel, invasion of the wall of the colon occurs, followed by peritonitis, septicemia, and finally vascular collapse and death, often within 24 to 48 hours. The seriousness of this condition cannot be underestimated; immediate vigorous management and resuscitative measures are indicated.

Swenson[25] noted that in infants who had a colostomy performed before the onset of enterocolitis, the mortality is 4 per cent. If the colostomy is done after enterocolitis has developed, the mortality is 33 per cent.

In the newborn or young infant the diagnosis can be made quite easily by barium enema by an experienced radiologist, but the configuration of the colon is different from that of the older child. Instead of a large colon which ends in a narrow aganglionic segment, the colon is more gradually tapered from large to narrow, so that the bowel appears to be funnel-shaped. A clear transition zone is often not seen (Fig. 5).

Rectal manometry, although more difficult in the infant, has been adapted for this age group and will also show a nonrelaxing internal anal sphincter.

Prompt colostomy should be performed in the neonate with Hirschsprung's disease. There is usually no need to do a rectal biopsy first because the clinical course and x-ray findings are reliable criteria for making the diagnosis. If the infant has enterocolitis and is septic, he must be treated quickly and aggressively to control the sepsis, dehydration, and hypoproteinemia. If there is considerable abdominal distention, nasogastric suction and dilatation of the anal sphincter often will produce sufficient decompression while the sepsis is being treated. Some surgeons suggest insertion of rectal tubes and washouts of the distal colon, but if the bowel is ulcerated the possibility of sepsis is enhanced and perforation may occur. Instead, several gentle rectal dilatations each day can aid evacuation of the colon.

Once the child's condition is stable, colostomy should be done. At this time the definitive diagnosis can be made by intraperitoneal biopsies of the colon. A small rectangular part of the muscle wall is excised

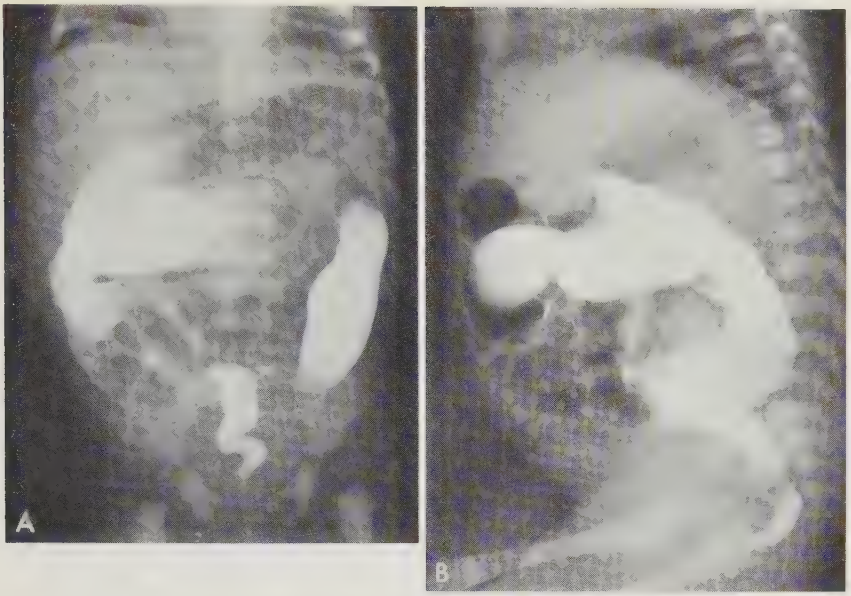

Figure 5. Newborn: Barium enema showing tapering of rectosigmoid with no clearcut transition zone.

down to the submucosal layer. It should include both longitudinal and circular layers of muscle and be big enough that the pathologist can use it for both frozen and permanent sections. The mucosa should not be entered, for fear of spilling liquid feces. Infiltrating the colon wall with saline using a #25 gauge needle facilitates taking a seromuscular biopsy without accidentally entering mucosa. Biopsies are taken from the aganglionic segment and also from the area of colon just above the transition zone where the colostomy is to be placed. As a guide, in the neonate there is no obvious or abrupt change from hypertrophied normal colon to aganglionic segment, but rather a tapering of the bowel at this point. The ganglionated colon has prominent tinea and visible longitudinal muscle fibers which gradually become less apparent as they merge into the transition zone. If the site chosen for colostomy shows the presence of ganglion cells on frozen section, a simple loop colostomy is constructed. It is very important to suture the colon to both the peritoneum and fascia, because of the propensity of the small intestine to eviscerate out around the colostomy postoperatively in children.[1] The colostomy is then opened at the end of the operation or the following day.

If the colostomy is placed just above the transition zone, at the time of the definitive pull-through procedure it can be taken down and used in the pull-through. However, the colostomy can be made in the right transverse colon if one wants to protect the anastomosis, especially in the Swenson procedure. This, of course, requires another operation for closure of the colostomy. If a right transverse colostomy is used it is important to be sure that there is enough length of normal bowel distal to

it to perform a pull-through procedure. For example, if the aganglionic segment extends higher than usual, i.e., to mid-descending colon, right-sided colostomy may be inadvisable, resulting in too short a length of colon to reach the perineum except by taking down the colostomy.

OPERATIVE PROCEDURES

Swenson reported in 1948[24] the operation which now bears his name (Fig. 6). He showed that after resecting the aganglionic segment, the anastomosis of normal colon to remaining rectum must not be higher than twice the width of the internal anal sphincter. If more than this length of aganglionic rectum is retained, i.e., more than 1.5 cm above the anus, there can be recurrence of all the symptoms and radiographic findings of the disease. This low anastomosis is performed from below by everting the distal rectum out of the anus. The normal proximal bowel is then intussuscepted through and anastomosed to the distal 1.5 cm. of rectum. The dissection must be meticulous, staying close to the rectal wall, in order to preserve the adjacent pelvic nerves. Complications include stricture, leaks and abscesses with a resulting frozen pelvis, neurogenic bladder and impotence from injury to pelvic nerves.

In 1952 State,[19] because of the problems which can accompany Swenson's procedure, reported a series of 15 patients on whom he performed a low anterior resection in order to preserve the innervation of the lower rectum. He believed that by removing all of the hypertrophied, dilated bowel, the remaining proximal undilated portion would be able to propel the fecal contents through a relatively long aganglionic segment. However, in a 10-year follow-up, 12 of his 18 patients showed dilatation of the remaining colon but no obstructive symptoms.[20]

In 1957 Duhamel[6] reported his operation aimed at preserving the innervation of the lower rectum and bladder by a wide side anastomosis of the aganglionic rectal segment to normal colon. The posterior half of the internal anal sphincter is opened enough by this retrorectal anastomosis so that even though the aganglionic segment remaining is long, the normally innervated proximal colon can push the fecal contents through the rectal conduit and pass the less spastic sphincter.

Various methods of accomplishing this anastomosis have been devised. Crushing clamps are used to necrose the intervening common rectal and colon walls; Grob modified the procedure by doing a low posterior resection and anastomosis by intussuscepting and suturing the bowel outside the anus; recently the GIA stapler* has been used.

The two significant complications following the Duhamel procedure concern the formation of a dilated anterior rectal pouch or stricturing from an enlarging septum between the rectum and colon. Both of these problems can be eliminated by several modifications in which the common septum is completely excised or the upper rectum is anastomosed to the side of the colon.

Soave[18] presented his procedure in 1961 in which an endorectal

*Auto Suture Corporation, New York, New York.

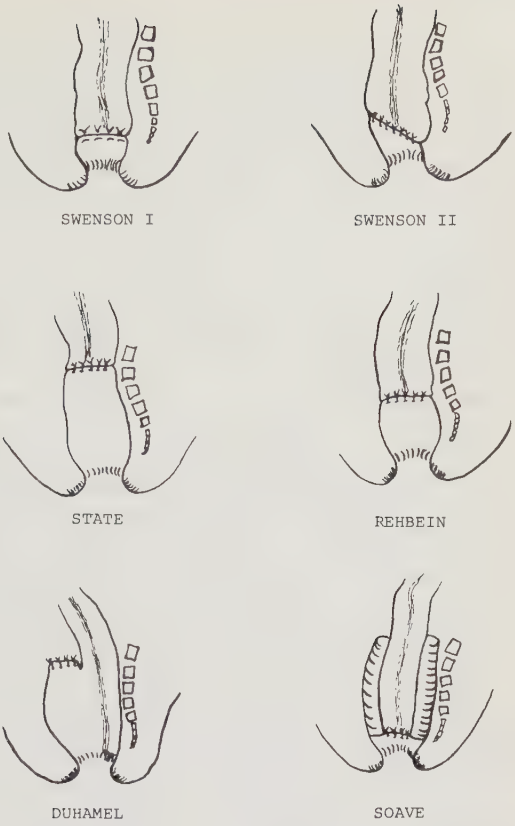

Figure 6. Diagram of various operative procedures for correction of Hirschsprung's disease.

anastomosis is achieved. The mucosa of the aganglionic rectum is removed from the pelvic brim to the anus and the normal proximal colon is pulled through the remaining aganglionic muscular sleeve. It is brought out through the anus for a distance of several centimeters and then is resected in 2 to 3 weeks after adequate sealing to the anal mucosa has occurred. Boley[3] modified this method by anastomosing the pulled through colon to the anus directly.

Because the sphincter is not damaged significantly by this procedure many patients have recurrence of their symptoms and require repeated dilatations or sphincterotomies. Other complications include stricture at the anastomosis, leaks, and abscesses.

Rehbein's[14] method consists of a very low anterior resection which is accomplished by means of a special retractor. Heavy silk sutures pull the pelvic floor up into the operative field and are attached to the retractor. A lower anastomosis is achieved but the internal anal sphincter is not damaged. These patients require frequent dilatations because of recurrence of their obstructive symptoms. Probably Rehbein's good results are due to the massive size of his bougies which succeed in tearing the sphincter enough to overcome its spasticity.

In 1964 Swenson[23] reported a modification of his pull-through procedure. Many of his postoperative patients developed transient periods of

intestinal obstruction or enterocolitis, most likely due to the fact that, because of his meticulous technique, the internal sphincter was not damaged sufficiently. Since many of these children were relieved by sphincterectomy, he changed his operative procedure by resecting the rectum 1 cm from the mucocutaneous line posteriorly and 2 cm anteriorly, thereby producing a diagonal line very similar to that in the Duhamel operation. This technique produced enough damage to the sphincter so that its spasm is relieved and obstruction is no longer a problem.

For many years Hirschsprung's disease has been classified as short segment, long segment, or total aganglionosis. The short segment involves a varying length of rectosigmoid and the long segment includes the left colon up to the splenic flexure. More recently a short segment type of Hirschsprung's is described which involves extremely short segments below the peritoneal reflection, some involving only the internal sphincter.

Many children with this type of short segment have been cured by a myomectomy which damages the internal anal sphincter sufficiently so that the obstructive spasticity of this muscle and the short aganglionic segment can be overcome by the proximal normal colon. A 1 cm wide full-thickness muscle layer is excised from the posterior portion of the internal anal sphincter and rectal wall. Nisson[11] believes it is not necessary to excise the full length of the short aganglionic segment since damaging the internal sphincter alone should be enough to reduce its spasticity and prevent further obstructive symptoms. This would of course hold true only for the very short segment. Normal proximal colon cannot overcome the obstruction produced by the longer segments even though a sphincterectomy is done.

A few patients with ultra short segments may be relieved by a generous rectal biopsy alone.

SUMMARY

Hirschsprung's disease or aganglionic megacolon is an anomaly caused by the absence of ganglion cells in the myenteric plexus of the distal colon. It produces intestinal obstruction or lethal enterocolitis in the neonatal period and constipation of varying degree in the older child.

The diagnosis can be made by history alone and confirmed by physical findings, barium enema, motility studies, and rectal biopsy. Colostomy may be a life saving measure in the newborn, to be followed by a definitive pull-through procedure before the age of 1 year. Operative correction consists of various techniques all of which aim for excision of the aganglionic segment with preservation of the internal anal sphincter. The major pitfall of these procedures is a too perfectly preserved sphincter which remains spastic and still produces obstruction. Some damage to this muscle must be accomplished either during the procedure or postoperatively by bouginage in order to obtain a satisfactory result.

REFERENCES

1. Bishop, H. C.: Colostomy in the newborn. Am. J. Surg., 101:642, 1961.
2. Bodian, M., Stephens, F. D., and Ward, B. C. H.: Hirschsprung's disease and idiopathic megacolon. Lancet, *1*:6–11, 1949.
3. Boley, S. J., Lafer, D. J., Kleinhaus, B. D., Mestel, A. L., and Kottmeier, P. K.: Endorectal pull-through procedure for Hirschsprung's disease with and without primary anastomosis. J. Ped. Surg., *3*:258, 1968.
4. Cameron, J. A. M.: On the aetiology of Hirschsprung's disease. Arch. Dis. Child., *3*:210–211, 1928.
5. Dalla Valle, A.: Richerche istologische su di un caso di megacolon congenito. La Pediatrica, *28*:740–752, 1920.
6. Duhamel, B.: Retrorectal and transanal pull-through procedure for the treatment of Hirschsprung's disease. Dis. Col. Rect., *7*:455, 1967.
7. Ehrenpreis, T., Norberg, K. A., and Wirsen, C.: Sympathetic innervation of the colon in Hirschsprung's disease: A histochemical study. J. Ped. Surg., *3*:43, 1968.
8. Finney, J. M. T.: Congenital idiopathic dilatation of the colon. Surg. Gynec. Obstet., *6*:624–643, 1908.
9. Gray, S. W., and Skandalakis, J. E.: Embryology for Surgeons. Philadelphia, W. B. Saunders Co., 1972, p. 187.
10. Hirschsprung, H.: Stuhltragheit Neugeborener in Folge von Dilatation und Hypertrophie des Colons. Jahrbuch f. Kinderheilk., *27*:1, 1887.
11. Nissan, S., Bar-Moar, J., and Levy, E.: Anorectal myomectomy in the treatment of short segment Hirschsprung's disease. Ann. Surg., *170*:969, 1969.
12. Norberg, K. A.: Transmitter histochemistry of the sympathetic adrenergic nervous system. Brain Res., *5*:125, 1967.
13. Okamoto, E., and Ueda, T.: Embryogenesis of intramural ganglia of the gut and its relation to Hirschsprung's disease. J. Ped. Surg., *2*:436, 1967.
14. Rehbein, F., and von Zimmermann, H.: Results with abdominal resection in Hirschsprung's disease. Arch. Dis. Child., *35*:29, 1960.
15. Robertson, H. E., and Kernohand, J. W.: The myenteric plexus in congenital megacolon. Proc. Mayo Clin., *13*:123–125, 1938.
16. Schnaufer, L., Talbert, J. L., Haller, J. A. Jr., et al.: Differential sphincteric studies in the diagnosis of anorectal disorders of childhood. J. Ped. Surg., *2*:538, 1967.
17. Schuster, M. M., Hookman, P., Hendrix, T. R., and Mendeloff, A. I.: Simultaneous manometric recording of internal and external anal sphincter reflexes. Bull. Johns Hopkins Hosp., *116*:79–88, 1965.
18. Soave, F.: Hirschsprung's disease: Clinical evaluation and details of a personal technique. Z. Kinderchir., *3*(Suppl.):66, 1966.
19. State, D.: Surgical treatment of idiopathic congenital megacolon (Hirschsprung's disease). Surg., Gynec. Obstet., *95*:203, 1952.
20. State, D.: Segmental colon resection in the treatment of congenital megacolon (Hirschsprung's disease). Am. J. Surg., *105*:93, 1963.
21. Stone, W. D., Hendrix, T. R., and Schuster, M. M.: Aganglionosis of the entire colon in an adolescent. Gastroenterology, *48*:636, 1965.
22. Swenson, O.: Pediatric Surgery 2nd ed. New York, Appleton-Century-Crofts, 1968, p. 388.
23. Swenson, O.: Partial internal sphincterectomy in the treatment of Hirschsprung's disease. Ann. Surg., *160*:540, 1964.
24. Swenson, O., and Bill, H. A., Jr.: Resection of the rectum and rectosigmoid with preservation of the sphincter for benign spastic lesions producing megacolon. Surgery, *24*:212–220, 1948.
25. Swenson, O., and Davidson, F. Z.: Similarities of mechanical intestinal obstruction and aganglionic megacolon in the newborn infant. N. Eng. J. Med., *262*:64, 1960.
26. Swenson, I., Shuman, J. O., and Fisher, J. H.: Diagnosis of congenital megacolon: An analysis of 501 patients. J. Ped. Surg., *8*:587, 1973.
27. Tiffan, M. E., Chandler, L. R., and Faber, H. K.: Localized absence of the ganglion cells of the myenteric plexus in congenital megacolon. Am. J. Dis. Child., *59*:1071, 1940.

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Omphalocele

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Omphalocele (exomphalos) is a defect of the abdominal wall at the umbilicus with herniation of abdominal contents. There may be a sac or not. The incidence is about 1 in 6000 live births.[25, 38] Credit has been given to Ambrose Paré for the first description,[34] and to Hey and Hamilton for the first successful closures.[19, 20]

Gastroschisis differs from omphalocele in that there is a normal insertion of the umbilical cord to the abdominal wall. Also, there is a paraumbilical full-thickness abdominal wall defect, and absence of a sac covering the herniated viscera. The incidence is about 1 in 30,000.[38] Although the first description appeared in 1557 in Lycosthenes' *Chronicon*,[4] the first successful surgical closure was reported only 30 years ago.[7]

The difficulties encountered in closing a large omphalocele or gastroschisis led initially to staged procedures with wide skin mobilization to cover the defect,[16, 33, 52] and more recently to the use of temporary prosthetic materials to accomplish closure in one hospitalization.[39] Due to these technical advances and associated with a better understanding of preoperative and postoperative care including transport, anesthesia, and nursing management and nutritional support, both omphalocele and gastroschisis have passed from being pathologic curiosities to entities with rapidly improving survival rates.[2, 5, 24, 25, 28-30, 35, 37, 43, 44, 51] More important, these infants develop into normal adults.

EMBRYOLOGY

Omphalocele

There is some controversy about the origin of omphalocele. Several authors feel that the basic defect is a failure of anterior extension of the lateral abdominal folds which eventually become the lateral abdominal walls. Because of the arrest in this extension, there is a continuous communication between the true abdomen and yolk sac through the umbi-

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licus. Intestines and other abdominal organs would occupy both spaces, depending on the size of the defect.[9, 17, 22] Others[14] feel that the fault lies in the arrest of the normal migration of the elongating intestines from the yolk sac into the true abdominal cavity. In either case, the arrest or teratogenic insult occurs at about the tenth week of gestation. Omphaloceles are sometimes associated with ectopia cordis and bladder extrophy.[10, 46] Arrested development of the cephalic fold as well as the lateral abdominal folds could explain ectopia cordis and other thoracic defects. Similarly, arrest of the caudal and lateral folds could explain the association with bladder exstrophy.

Gastroschisis

There is more controversy about the origin of gastroschisis since the presentation is usually a small full-thickness opening to the right of the umbilicus through which is protruding the uncovered intestines. Gray and Skandalakis[14] feel that gastroschisis is a true herniation of the abdominal contents through a congenital muscular defect in the abdominal wall. The primary defect lies in the failure of the mesoderm migrating from the dorsal myotomes to become part of the anterior abdominal wall and that no skin forms because lacking a mesodermal support, the ectoblastic layer is reabsorbed. This leaves a full-thickness defect in the abdominal wall lateral to the umbilicus.[9, 22] In 1894, Teruffi[47] classified gastroschisis into seven categories depending upon the portion of the anterior abdominal wall included by the defect. This classification has not been used extensively.

Shaw recently challenged the generally accepted embryogenesis of gastroschisis.[40] According to his theory, this entity occurs following in utero rupture of the membrane that normally encloses the umbilicus after the completion of the infolding of the anterior abdominal wall components, but prior to complete closure of the umbilical ring.

DIAGNOSIS

The diagnosis in both omphalocele and gastroschisis is usually obvious. In the former, there is a defect involving the base of the umbilical cord which can be quite small (Fig. 1). The small ones often contain just a portion of the small and large intestine whereas the large ones may often times contain the liver (Fig. 2). Usually, omphaloceles are covered by the remnant of the extraembryonic coelom, but occasionally intrauterine rupture occurs and there is no covering. The differentiation of this anomaly from gastroschisis may be difficult. A word of warning about the very small omphalocele. There have been several reports[25, 49] where the umbilical cord was clamped very close to the anterior abdominal wall, across an occult omphalocele, resulting in small bowel obstruction, intestinal atresia, and intestinal-umbilical fistulae. This can be avoided by placing the umbilical cord tie or clamp several centimeters distally on the umbilical cord.

Gastroschisis will have a normal insertion of the umbilical cord with a lateral abdominal wall defect, usually to the right of the umbilicus and

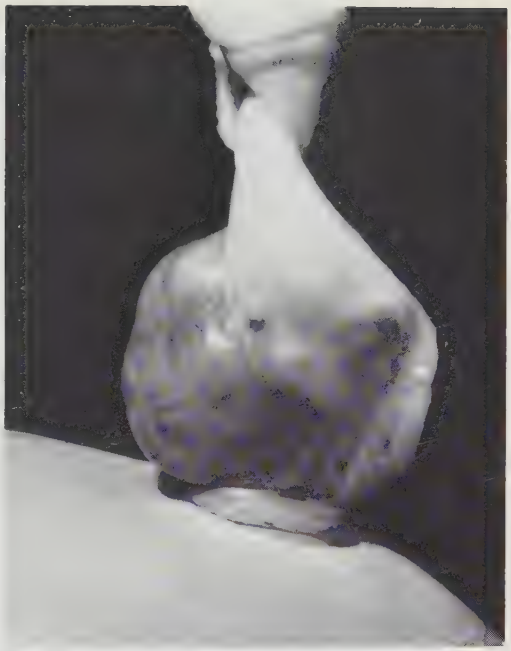

Figure 1. A small omphalocele involving the base of the umbilicus. Careless application of the umbilical cord clamp across a less obvious sac could be disastrous.

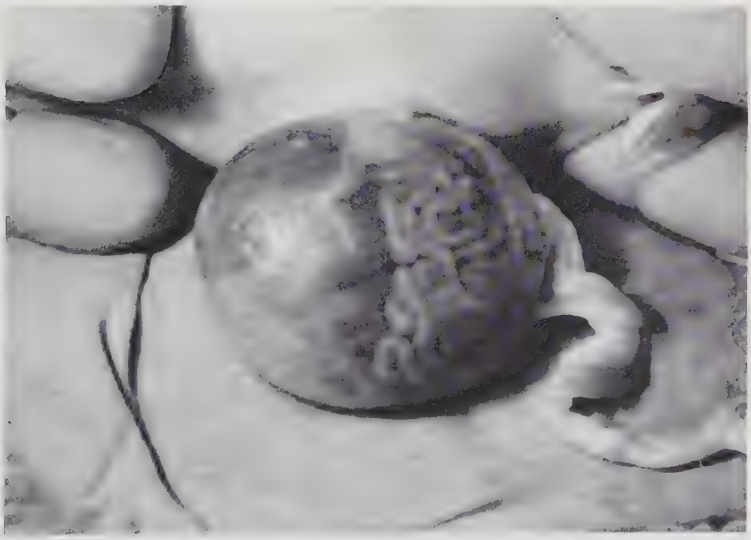

Figure 2. A large omphalocele. Note the insertion of the umbilical cord. The contents contain the liver and the nonrotated small and large intestines.

Figure 3. Gastroschisis. Note the normal insertion of the umbilical cord, the relatively small abdominal wall defect, and the absence of a sac.

with no evidence of hernia sac present (Fig. 3). Usually, the small and large intestines are eviscerated. We have seen two cases where undescended testicles were eviscerated as well. Laboratory models of gastroschisis have been created in the fetal rabbit[41] and fetal lamb.[18] The apparent foreshortening, thickening, and brawny induration seen in the human infant[13] can be duplicated in both laboratory models. There is histologic similarity, as well. It is of interest, that once the intestine has been removed from the amniotic fluid and placed in its natural habitat, at least in the experimental animal, the apparent short bowel present returns to a normal length intestine. Also, the longer the intestine is exposed to amniotic fluid, the more thickening, induration, and foreshortening noted. Occasionally, because of the associated malrotation, the entire eviscerated intestine is strangulated at birth.[26]

ASSOCIATED ABNORMALITIES

Rickham[38] noted 205 associated malformations in 83 cases of omphalocele. The most commonly involved system was the gastrointestinal tract. Malrotation of the intestine was present in the majority of cases. In decreasing frequency were Meckel's diverticulum, patent omphalomesenteric duct, intestinal atresia or stenosis, malrotation with volvulus, intestinal duplication, meconium ileus, and biliary atresia.

Fifty-three patients had genitourinary malformations and 18 patients had intrathoracic malformations, of which 16 were congenital heart defects. There were anomalies of the jaw and tongue, tumors and hemangiomata, limb anomalies, inguinal hernias, absent abdominal musculature, and several cranial, ophthalmic, and vertebral anomalies.

In gastroschisis, associated anomalies were much less common. Those noted involved the gastrointestinal tract. Prematurity occurred in about one-third of cases in both omphalocele and gastroschisis.

Hutchin and Goldenberg[23] reported an incidence of 79 per cent associated anomalies in their series.

TREATMENT

Initial

It is imperative to transport these infants as soon as possible to a surgical center. However, there are certain measures that will insure the patient's safe arrival and ability to tolerate immediate major surgery. Hypothermia is the most immediate problem. Covering the exposed sac or eviscerated intestines with warm saline-soaked sponges and then wrapping the baby with circumferential sterile gauze rolls will prevent drying out and help reduce heat loss. Plastic sheets will further reduce heat loss. In gastroschisis, great care should be taken that the intestines are not twisted underneath the gauze dressing, which can cause compromise of the vascular supply to the eviscerated bowel. Placing the infant in an incubator will further lessen heat loss. Recently, plastic bags containing warm physiologic solutions have been used to transport these infants. The lower portion of the patient is placed in the bag which is then closed above the defect. Warm solutions are added. In the case of gastroschisis, the intestines may float. Since the bags are transparent, the infant can be observed easily and any twisting of intestines without a hernia sac can be noted readily.

A nasogastric tube, #8 or #10 French, should be passed into the infant's stomach to prevent vomiting with its complication of aspiration and to prevent further distention of the stomach and intestines. Oxygen should be administered to the infant. One should always check that vitamin K has been administered to the infant. Sometimes in the excitement of the delivery, the routine administration of vitamin K is overlooked. Intravenous fluids may or may not be necessary during the immediate postnatal period or during transport. If acidosis is severe, a cutdown placed in the antecubital fossa with administration of appropriate physiologic solutions and sodium bicarbonate will correct the problem. Upon arrival, a chest x-ray, KUB, upright film of the abdomen, and lateral abdominal film will be useful to rule out other associated anomalies.

Nonoperative Management

Since Ahlfeld[1] first used a 2 per cent solution of Mercurochrome to paint the sac and allow scarring, contracture, and epithelialization, a number of centers have used this technique in the very large omphaloceles,[7, 8, 15, 45] with 28 survivors out of 34 patients. Firor has used aqueous Zephiran or 70 per cent alcohol in a similar fashion.[12] Polyethylene sheets[53] and allografts[27] have also been used to temporarily cover the vulnerable sac. These techniques allow for the development of a ventral hernia which can then be repaired at a later date.

One must be aware that any agents painted on an intact sac can be absorbed systemically and if in toxic concentration may be lethal or cause severe growth and development abnormalities. Another disadvantage is that there is no inspection of the abdominal contents and therefore unsuspected congenital malformations such as intestinal atresia may be missed.[32] Seldom should such treatment of an omphalocele be needed today.

Primary Closure

Small omphaloceles can usually be closed primarily. In gastroschisis, it is rare to close one primarily[36] unless there has only been a short exposure to amniotic fluid with less edema and thickening of the extruded viscera.

In a small omphalocele, the thinned out sac and umbilicus are excised and the abdominal contents inspected. The defect may have to be enlarged in the very small cases. The malrotation is confirmed and the appendix is removed to avoid appendicitis with its atypical presentation later in life. If a Meckel's diverticulum is present, this is also removed. The intestine is fixed to prevent volvulus. A layered closure using nonabsorbable suture material to the peritoneum and fascia is then carried out. If relaxants are used for anesthesia and there is some question of either respiratory embarrassment from elevation of the diaphragm or decreased cardiac output from vena cava compression, the agent should be reversed and the child allowed to regain muscular tone. Often, one can increase the size of the abdominal cavity by stretching the abdominal walls manually.[35] This often will give enough room so that respiratory or cardiovascular embarrassment is avoided.

A Stamm gastrostomy may or may not need to be done depending upon the size of the defect, associated anomalies, and the length of time before the gastrointestinal tract functions normally. Remember, a nasogastric tube compromises one half the airway in a normal infant so that if prolonged ileus is anticipated, a gastrostomy tube should be inserted.

Partial hepatectomy[6] or partial small bowel resection[31] to reduce the abdominal contents being returned to the abdomen should never be done.

Two-Stage Repair

This repair, usually in large defects, consists of excising the umbilicus with or without leaving the sac intact and mobilizing skin flaps widely to cover the hernia defect. This method was first recommended by Olshausen in 1887.[33] Later, Williams[52] and, more recently, Gross[16] used this method successfully. This creates a ventral hernia which can be repaired at a later date. One disadvantage is that if the sac is not opened, the abdominal contents are not inspected and other anomalies are missed. A second disadvantage is that massive adhesions usually occur between the omphalocele sac and the intestines, making a second-stage repair difficult. This technique proved to be life-saving for many children where primary closure was impossible but since the ventral hernia seemed to enlarge more than the peritoneal cavity, the second-

stage procedure often proved to be as hazardous in the older child as in the newborn. It is an outmoded method today.

Staged Repair with Silastic Sheeting

Although plastic sheeting had been used in the nonoperative management of large omphaloceles,[53] the operative use was first described by Schuster using Silastic-coated Teflon mesh.[39] Using this technique complemented by the introduction of total parenteral nutrition,[11] the survival of infants with large omphaloceles and gastroschisis has dramatically improved.

With a large omphalocele, the umbilicus and thin membrane are excised. Inspection of the abdominal cavity rules out other anomalies. A gastrostomy is also done and brought out through a stab wound in the left upper quadrant for gastrointestinal decompression. The skin and subcutaneous tissue are mobilized only enough to expose underlying fascia and muscles. Two sheets of Silastic sheeting are sutured to the full-thickness fascia and muscle on opposite sides of the defect, using interrupted nonabsorbable suture material. The two sheets are then sutured together with minimal tension so that when the infant awakens from anesthesia, there will be no cardiorespiratory compromise. Dressings are then applied, such as Xeroform gauze, to the sheeting, Betadine ointment at the junction of sheeting and abdominal wall, and dry sterile dressings. Parenteral antibiotics like oxacillin and kanamycin or gentamycin are given.

At 1 or 2 day intervals under no anesthesia, the patient is returned to the operating room where the Silastic sheeting is tightened under sterile conditions. Often, 50 per cent of the mesh can be removed after only 24 hours time. Optimum tightening is seen immediately since the patient is fully awake. Some surgeons shorten the mesh in the nursery in the incubator, but we prefer a sterile operating room. In 7 to 14 days, depending upon the size of the original defect, the remaining mesh is shortened. Final closure of the abdomen in layers, with removal of remaining mesh, is done under anesthesia. Skin closure is delayed for 2 days since there usually is bacterial contamination by then. Figure 4 shows the various stages in the closure of a large omphalocele. When the sheeting has reached a critical size so that clamps cannot be applied to decrease the size of the remaining material, but where the patient is not ready to have the remaining prosthesis excised with a layered closure, Shim[42] has used plication of the Silastic sheeting to further reduce the size.

Total intravenous nutrition is often started the day after surgery, administering fat (Intralipid) and amino acid-sugar mixtures through peripheral veins. Central intravenous nutrition is used in most cases where caloric requirements cannot be met by peripheral intravenous alimentation or when peripheral intravenous sites become depleted. Insertion of a superior vena cava catheter by either percutaneous puncture of the internal jugular vein or by cutdown procedure will allow administration of sufficient calories (about 125 cal per kg per day) so that the patient is in an anabolic state. This allows for growth and develop-

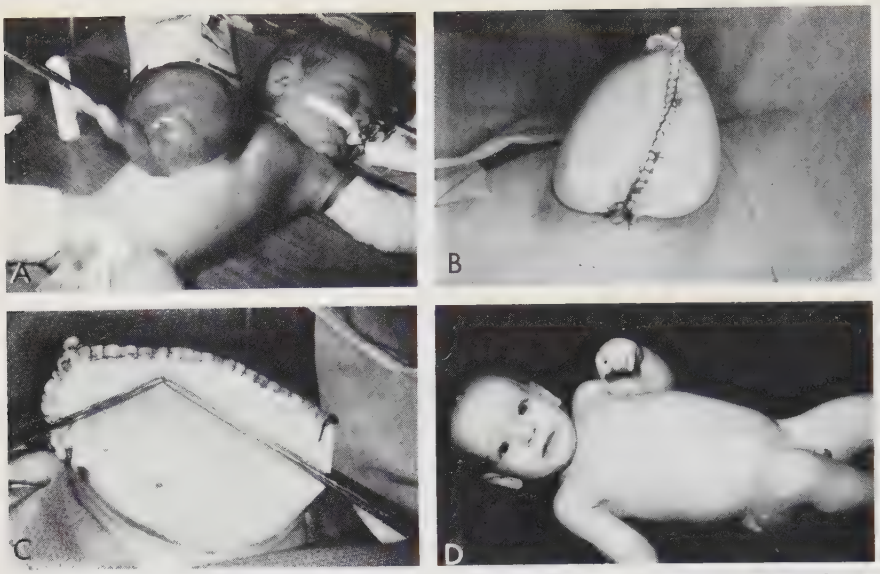

Figure 4. *A*, Large omphalocele containing liver. *B*, Silastic sheeting in place without tension. *C*, Shortening the Silastic. This procedure is done under no anesthesia to avoid closing it too tightly, which can cause respiratory distress and decreased venous return. *D*, The patient at 3 months of age.

ment, aids in wound healing, and perhaps promotes earlier gastrointestinal function.

The Silastic sheeting has been especially successful in increasing the survival of patients with gastroschisis. Too small an abdominal cavity combined with thick, matted, contaminated loops of bowel contributed to a very high mortality. Using Silastic sheeting the intestine can be returned to the abdomen in a much shorter period of time. Interestingly, the bowel and mesentery loses its induration and edema once it is returned to the abdominal cavity[18] though ileus can be present for several weeks. Infection has not been a major problem. In follow-up studies, the bowel which was thought to be foreshortened appears to be of normal length.[48] Gastrostomy is always done. Total intravenous nutrition is started immediately since normal gastrointestinal function often may not appear for weeks. If the abdominal wall defect is small, it should be enlarged to avoid vascular compromise of the eviscerated bowel. If the defect is large, the Silastic mesh can be sutured directly to the fascia and muscle using nonabsorbable suture material and a tower (Silon silo) can be constructed. Twisting the long narrow tower every 1 or 2 days without anesthesia and using heavy silk ligatures will shorten the Silastic sheeting quickly. This is done under sterile conditions and may be done more easily than reducing the Silastic mesh on a large omphalocele. Figure 5 shows one case from admission to completion.

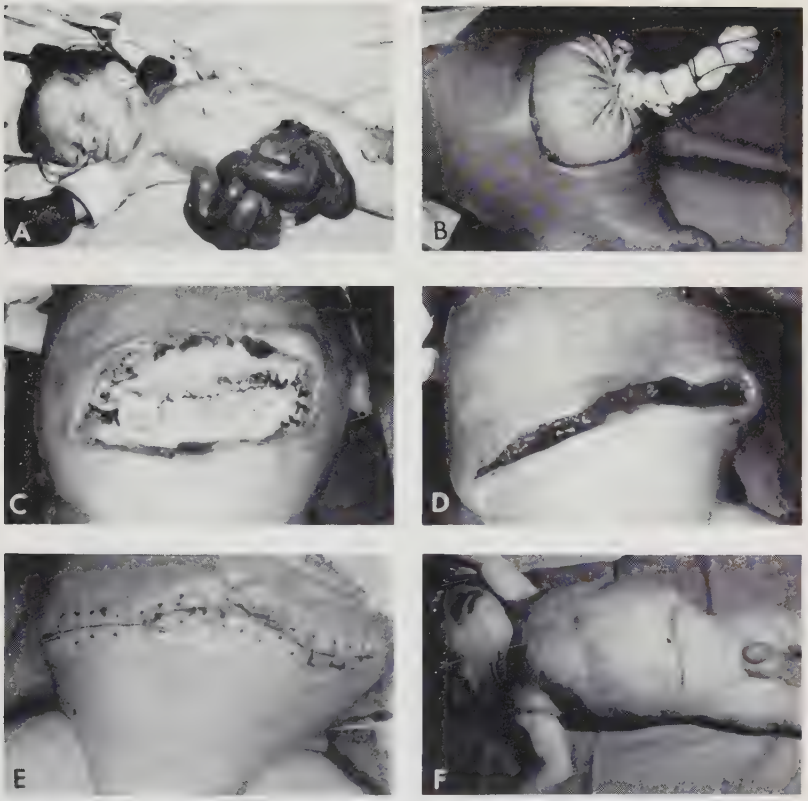

Figure 5. *A*, Gastroschisis. Note the thickened, edematous foreshortened, nonrotated intestines. *B*, Silastic silo. Note silk ligatures used to force gut from silo into gradually enlarging peritoneal cavity. *C*, Ready for excision of remaining Silastic and layered closure. *D*, Abdomen closed. The skin closure is delayed for 72 hours. *E*, Skin closure. *F*, The patient several weeks after discharge.

RESULTS

The improved survival rates are most striking in the management of large omphalocele and gastroschisis. Hollabaugh and Boles[21] reported that prior to 1967 only six out of 20 patients survived, whereas since that time, 19 of 27 lived. Other authors report greater than a 75 per cent survival rate using Silastic prosthesis.[3, 29, 51]

The advantages of the Silastic closure are numerous. The normal growth and development of the child is not impeded by large ventral hernias, abnormal body habitus, or future hospitalizations. It is of inestimable importance that a well child be presented to the parents upon discharge from the hospital.

SUMMARY

From a historical curiosity at the turn of the century, today omphalocele and gastroschisis can be corrected with good results, thanks to innovative techniques and better understanding of the newborn. Associated anomalies consist mainly of malrotation, Meckel's diverticulum, intestinal atresia, congenital heart defects, and genitourinary abnormalities. Nonoperative management in certain centers has been successful for the very large omphaloceles with an intact sac; however, a secondary procedure is necessary. In the past 10 years, the use of Silastic sheeting and total parenteral nutrition has allowed early repair of even the most severe cases, with excellent end results and low mortality.

REFERENCES

1. Ahlfeld, F.: Der Alkohol bei der Behandlung inoperabeler Bauchbrueche. Wschr. Geburtsh. Gyn., *10*:24, 1899.
2. Aitken, J.: Exomphalos. Arch. Dis. Child., *38*:126, 1963.
3. Allen, R. G., and Wrenn, E. L.: Silon as a sac in the treatment of omphaloceles and gastroschisis. J. Ped. Surg., *4*:3, 1969.
4. Ballantyne, J. W.: The Embryo. *In* Manual of Antenatal Pathology and Hygiene. Edinburgh, 1904.
5. Bill, A. H.: Hernias other than inguinal. *In* Mustard, W. T., Ravitch, M. D., Synder, W. H., Jr., et al. (eds.): Pediatric Surgery, Vol. I. Chicago, Yearbook Medical Publishers, 1969.
6. Buchanan, R. W., and Cain, W. L.: A case of complete omphalocele. Ann. Surg., *143*:552, 1956.
7. Cunningham, A. A.: Exomphalos. Arch. Dis. Child., *31*:144, 1956.
8. Drescher, E.: Observations on the conservative treatment of exomphalos. Arch. Dis. Child., *38*:135, 1963.
9. Duhamel, B.: Embryology of exomphalos and allied malformations. Arch. Dis. Child., *38*:142, 1963.
10. Eraklis, A. J., Trump, D. S., and Longino, L. A.: Omphalocele with diaphragmatic and pericardial defects: diagnosis and repair. J. Ped. Surg., 2:354, 1967.
11. Filler, R. M., Eraklis, A. J., Das, J. B., et al.: Total intravenous nutrition: An adjunct to the management of infants with ruptured omphalocoele. Am. J. Surg., *121*:454, 1971.
12. Firor, H. V.: Omphalocoele—an appraisal of therapeutic approaches. Surgery, 69:208, 1971.
13. Gilbert, M. G., Mencia, L. F., and Puranik, S. R.: Management of gastroschisis and short bowel: report of 17 cases. J. Ped. Surg., 7:598, 1972.
14. Gray, S. W., and Skandalakis, J. E.: The anterior body wall. *In* Embryology for Surgeons. Philadelphia, W. B. Saunders Co., 1972, p. 410.
15. Grob, M.: Conservative treatment of exomphalos. Arch. Dis. Child., *38*:148, 1963.

16. Gross, R. E.: A new method for surgical treatment of large omphalocoeles. Surgery, *24*:277, 1948.
17. Gross, R. E.: Omphalocele (umbilical eventration). *In* The Surgery of Infancy and Childhood. Philadelphia, W. B. Saunders Co., 1953, p. 406.
18. Haller, J. A., Jr., Kehrer, B. H., Shaker, I. J., et al.: Studies of the pathophysiology of gastroschisis in fetal sheep. J. Ped. Surg., *9*:527, 1974.
19. Hamilton, J.: The Anatomy and Surgical Treatment of Crural and Umbilical Hernia. London, Longmans, 1806.
20. Hey, W.: Practical Observations in Surgery, London, T. Cadell and W. Davies, 1814.
21. Hollabaugh, R. S., and Boles, E. T.: The management of gastroschisis. J. Ped. Surg., *8*:263, 1973.
22. Hutchin, P.: Somatic anomalies of the umbilicus and anterior abdominal wall. Surg. Gynec. Obstet., *120*:1075, 1965.
23. Hutchin, P., and Goldenberg, I. S.: Surgical treatment of omphalocele and gastroschisis. Arch. Surg., *90*:22, 1965.
24. Izant, R., Brown, F., and Rothman, B. F.: Current embryology and treatment of gastroschisis and omphalocoele. Arch. Surg., *93*:49, 1966.
25. Johnson, A. H.: Omphalocoele and related defects. Am. J. Surg., *114*:279, 1967.
26. Kiesewetter, W. B.: Gastroschisis. Arch. Surg., *75*:28, 1957.
27. Kling, S.: Massive omphalocoele: A method of treatment employing skin allograft. Can. J. Surg., *10*:445, 1967.
28. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood. Philadelphia, W. B. Saunders Co., 1941, p. 314.
29. Lewis, J. E., Jr., Kraeger, R. R., and Davis, R. K.: Gastroschisis: ten years' review. Arch. Surg., *92*:218, 1973.
30. Mahour, G. H., Weitzman, J. J., and Rosenkrantz, J. G.: Omphalocoele and gastroschisis. Ann. Surg., *177*:478, 1973.
31. Meltzer, A.: Huge omphalocele ruptured in utero. J.A.M.A., *160*:756, 1956.
32. Moore, T. C.: Gastroschisis with antenatal evisceration of intestines and urinary bladder. Ann. Surg., *158*:263, 1963.
33. Olshausen, R. Z.: Zur Therapie der Nabelschnurhernien. Arch. Gyn. (Berlin), *29*:443, 1887.
34. Paré, A.: The Works of That Famous Chirurgion. London, Th. Cotes and R. Young, 1634.
35. Raffenberger, J. G., and Jona, J. L.: Gastroschisis. Surg. Gynec. Obstet., *138*:230, 1974.
36. Reed, E. N.: Infant disemboweled at birth—appendectomy successful. J.A.M.A., *61*:199, 1913.
37. Rickham, P. P.: Rupture of exomphalos and gastroschisis, Arch. Dis. Child., *38*:138, 1963.
38. Rickham, P. P.: Exomphalos and gastroschisis. *In* Rickham, P. P., and Johnson, J. H. (eds.): Neonatal Surgery. London, Appleton-Century-Crofts, 1969, p. 254.
39. Schuster, S. R.: A new method for the staged repair of large omphaloceles. Surg. Gynec. Obstet., *125*:837, 1967.
40. Shaw, A.: The myth of gastroschisis. J. Ped. Surg., *10*:235, 1975.
41. Sherman, N. J., Asch, M. J., Isaacs, H., Jr., et al.: Experimental gastroschisis in the fetal rabbit. J. Ped. Surg., *8*:165, 1973.
42. Shim, W. K. T.: Lateral plication of synthetic sack for large gastroschisis and omphalocele defects. J. Ped. Surg., *6*:143, 1971.
43. Simpson, T. E., and Lynn, H. B.: Omphalocoele: results of surgical treatment. Mayo Clin. Proc., *43*:65, 1968.
44. Smith, W. R., and Leix, R.: Omphalocoele. Am. J. Surg., *111*:450, 1966.
45. Soave, F.: Conservative treatment of giant omphalocoele. Arch. Dis. Child., *38*:130, 1963.
46. Spitz, L., Bloom, K. R., Milner, S., and Levin, S. E.: Combined anterior abdominal wall, sternal, diaphragmatic, pericardial, and intracardiac defects: a report of 5 cases and their management. J. Ped. Surg., *10*:491, 1975.
47. Taruffi, G.: Storia. Della Tetatologia, *7*:403, 1894.
48. Touloukian, R. J., and Spacman, T. J.: Gastroschisis—function and radiographic appearance following gastroschisis repair. J. Ped. Surg., *6*:427, 1971.
49. Vassy, L. E., and Boles, E. T., Jr.: Iatrogenic ileal atresia secondary to clamping of an occult omphalocele. J. Ped. Surg., *10*:797, 1975.
50. Watkins, D. E.: Gastroschisis. Virginia Med. Mon., *70*:42, 1943.
51. Wayne, E. R., and Burrington, J. D.: Gastroschisis. Am. J. Dis. Child., *125*:218, 1973.
52. Williams, C.: Congenital defects of the anterior abdominal wall, SURG. CLIN. N. AM., *10*:805, 1930.
53. Wollenweber, E. J., and Coe, H. E.: Conservative management of eventration in the newborn with survival. Am. J. Surg., *97*:769, 1959.

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Biliary Obstruction in the Newborn

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Looking at the problem of biliary atresia from the vantage point of 30 years' experience with the lesion, we can say with certainty that the jaundiced baby who has had no extrahepatic bile duct has been the most disappointing patient for the surgeon in the whole realm of lesions theoretically correctable by a surgical procedure.

Sidney Gellis was correct, I believe, in his conclusion that the chance of finding remnants of extrahepatic bile ducts in a jaundiced baby with biliary atresia was so slim that it was preferable to concentrate on the protection of the infant with neonatal hepatitis.[7] I came to the same conclusion on the basis of personal experience. After treating more than 150 jaundiced babies, I had found only five anatomic situations amenable to surgical correction. Four of these survived. One of them was not operated upon until after the age of 1 year, exploding for me the myth that biliary atresia patients in those days had to be operated upon before the age of 3 months in order to avoid a relentless cirrhosis of the liver. That young lady recovered completely, has never shown signs of hepatic dysfunction by laboratory tests, and had a subsequent needle biopsy of the liver which showed no cirrhosis.

Older Concerns

Were it not for the recent contributions from Japanese pediatric surgeons, particularly those of Morio Kasai in Sendai, we would probably still be muddling along in the treatment of the jaundiced baby.[2, 4] Historically, there was an era when the surgeon spoke of intrahepatic biliary atresia and extrahepatic biliary atresia. The intrahepatic variety had no visible external bile ducts and under the microscope, the liver showed no bile ducts capable of transporting bile. The so-called extrahepatic atresias had either no visible external bile ducts while the hepatic histology showed some intrahepatic ducts or there was an obvious atresia in the extrabiliary duct with a dilated, hypertrophied, proximal segment and an absent distal segment. This latter extremely rare variety was the only one for which an operative procedure could produce a cure.

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Several decades ago, it was accepted by those who worked with biliary atresia that infants with intrahepatic atresia lived longer than infants with extrahepatic atresia. Kasai disproved this while working with a number of successive liver biopsies from patients with various types of biliary obstruction that we had collected over the years at the Children's Hospital of Philadelphia. He showed that if a patient with extrahepatic biliary atresia lived long enough, his so-called extrahepatic biliary atresia microscopically became the picture of intrahepatic biliary atresia as his cirrhosis effectively eliminated the intrahepatic bile ducts. So, for purposes of this discussion, one might remember that Kasai proved that the intrahepatic histologic picture of biliary atresia was a dynamic one rather than a static one.

Working with our material, Verhagen showed that approximately 50 per cent of our patients with a diagnosis of biliary atresia for whom no surgical procedure could be done died within the first year. Another 25 per cent died before the end of the second year of life. The remaining 25 per cent lived on for varying periods, one youngster going as long as 9 years. The longevity of some patients with biliary atresia has never been adequately appreciated by many investigators working with jaundiced babies. For that reason operative procedures that logically could have never been expected to succeed were thought to be successful because the investigators assumed that survival for more than a year was due to the procedure in question.

Among the several foolish procedures that surgeons tried in their frustration to overcome their inability to deal with biliary atresia was an anastomosis between the cut surface of the liver and a loop of jejunum—a so-called hepaticoenterostomy. I have autopsied such patients operated upon by me and by several preeminent American surgeons; all were jaundiced, all had non-bile producing scar on the cut surface of the liver and a piece of bowel that was nonfunctional in reference to its intended purpose.

Kasai's Contributions

It was probably because of the fact that pediatric surgeons knew that a porticoenterostomy did not work, that no one really believed Kasai when he talked about his operation as long as 15 years ago. When he said he anastomosed the bowel to the porta of the liver, it was assumed by many (including me) that he was performing an hepaticoenterostomy.

Several years ago before the flurry of interest in the various Japanese reports and particularly in Kasai's operation, the situation in reference to the jaundiced baby was this: after hematologic causes for jaundice were ruled out and the jaundice was known to be obstructive, the surgeon's role was diagnostic as well as possibly therapeutic. Because of the concern over a delay in correcting a possibly correctable biliary atresia after the age of 3 months, most jaundiced babies were operated upon sometime during the third month of life. Usually a small abdominal incision was made in the vicinity of the gallbladder and if a gallbladder were present, a cholangiogram was done on the operating

table. A liver biopsy was taken at the same time. If the cholangiogram showed patency of ducts between the liver and the duodenum, the diagnosis was assumed to be neonatal hepatitis and the liver biopsy almost always confirmed this clinical cholangiographic impression. This was not always the case because the liver histology in some of these jaundiced babies is most difficult to interpret.

On the other hand, if the operating surgeon found no gallbladder, he had reason to believe that there was some disruption in the extrahepatic biliary system and was justified in doing a wider exploration of the porta of the liver. In practically every case no visible bile ducts were found and the patient was diagnosed as biliary atresia and was consigned to an eventual death which would be complicated if the patient lived long enough by the problems of excessive calcium excretion, the clinical problem of severe itching, and the eventual development of portal hypertension with all of its sequelae.

The first clue that the Japanese were talking about something other than the rest of the world was talking about came when Dr. Kasai produced photomicrographs of the liver hilum to which he had anastomosed the bowel by a variety of methods. There in the midst of areolar tissue and collagen fibers were true bile ducts. Dr. Kasai was *not* operating on biliary atresia. Dr. Kasai's operation will do *nothing* for biliary atresia. Dr. Kasai was operating on *biliary hypoplasia.*

Up until that time there were occasional patients who had minuscule extrahepatic ducts and these were called patients with biliary hypoplasia. Any series of biliary atresias of considerable size contained a few patients with very tiny but nevertheless present extrahepatic bile ducts.

Obviously, we have to stop calling this lesion which is amenable to portoenterostomy "biliary atresia." Atresia means no lumen. If no lumen exists, no operation will drain bile from the liver to the bowel.

A Surgical Plan of Attack

Dr. Benjamin Landing suggested[6] that we need a different approach to neonatal hepatitis and biliary atresia. I would suggest that we start with jaundice and then ruling out hemolysis, talk of obstructive jaundice. In our present state of knowledge, an operative cholangiogram may be necessary to make an accurate diagnosis. This should be done before the end of the second month of life if Kasai is correct.[1, 3]

At operation in a jaundiced infant a cholangiogram is mandatory if a gallbladder is present. If there is no gallbladder, or if the cholangiogram shows no extrahepatic ducts, a further exploration of the porta is certainly indicated. If no extrahepatic ducts are visible to the naked eye and the Kasai operation is performed, success will depend upon several things: first of all there must be a liver with intact intrahepatic ducts delivering bile to the porta. Secondly, bile ducts must be present in the tissue at the porta to which the anastomosis is done. Thirdly, a successful anastomosis must be carried out. Fourthly, ascending cholangitis must be prevented. Finally, if the patient is to survive without jaundice and cirrhosis, there must be eventual enlargement of these bile ducts.

There is still a corner of my mind which wonders how many patients who get well with the Kasai operation might get well without it. I know of no way to study this question.

The reason that I have this wonder is my knowledge that several preeminent pediatric surgeons who have technical ability, judgment, and integrity above reproach have operated upon infants who have had no *visible* extrahepatic bile ducts and have closed the abdomen expecting an eventual fatal outcome, only to be surprised to see the child lose his jaundice, grow and develop normally, and have no further difficulty. This seems to suggest that there are anatomic variants amenable to cure by the Kasai operation who get along without it. The fact that all patients who meet the aforementioned conditions do not get well introduces a credibility problem which is difficult to override.

Just as Kasai showed that the intrahepatic biliary system underwent dynamic change in going from what was called extrahepatic to intrahepatic biliary atresia, he seems to imply the same thing now in reference to extrahepatic bile ducts. If we understand Kasai correctly, it seems evident that there is an extrahepatic dynamic process at work which renders the portoenterostomy inoperable if the opportunity is not used advantageously early enough in the life of the jaundiced infant.[4]

It is certainly clear that Kasai is not operating upon biliary atresia. He knows it and we know it, and yet many persist in calling this pathologic entity biliary atresia when we are really dealing with biliary hypoplasia. Yet in view of the dynamic situation described by Kasai (both inside and outside the liver), the term biliary hypoplasia alone does not answer the question of nomenclature. We see patients whose operative cholangiograms show visible ducts of small caliber and we also call this biliary hypoplasia with early hepatic fibrosis or with hepatic cirrhosis and ductal proliferation or we call it neonatal hepatitis. Some of these patients go on to die; others put out bile and have variable courses postoperatively in reference to their jaundice and its clearing as well as in the progression of the hepatic fibrosis. Kasai describes hypoplasia so far advanced that the ducts are not visible to the naked eye as cords with lumina. I have suggested previously that we call the lesion that Kasai operates upon successfully "progressive extrahepatic biliary obstruction of the newborn."[5]

I am convinced that the hypoplasia we see on cholangiography and the hypoplasia Kasai operates upon successfully are not the same lesion, at least in severity. I am not sure at this juncture whether they represent stages in the progressive obstruction already alluded to. I suggest that they possibly do and that they and true biliary atresia and the neonatal hepatitis, as we call it, are all different facets of the same in utero insult to the fetal liver by some agent, perhaps a virus.

Surgical Procedures in Neonatal Jaundice

In conclusion, I believe that there are the following biliary obstructive lesions that pediatric surgeons might be called upon to manage in the early months of life:

1. *Extrahepatic discontinuity of the biliary tree* (the old lesion which we called biliary atresia), due to a developmental accident to the extrahepatic biliary tree. The liver shows the same histologic picture as in acquired obstruction in the older infant or child. These lesions are correctable. Unfortunately, they are extremely rare.

2. *Biliary hypoplasia*, as diagnosed by operative cholangiogram. The ducts are smaller than normal to microscopic in size. The hepatic histology shows variation in severity of cirrhosis and ductal proliferation. Perhaps here, surgical judgment must decide whether Kasai's operation or a period of watchful waiting, perhaps accompanied by steroid therapy, is a sensible plan to be followed. If there is no loss of jaundice in 3 to 4 weeks, reexploration and the Kasai operation seem indicated in the present state of our lack of knowledge.

3. *No extrahepatic ducts visible to the naked eye.* Some of these will have microscopic lumina in biliary cords and will respond to the Kasai operation in accordance to the stage of the obstruction, the histologic status of the liver, the skill with which the operation is performed, and the absence of eventual postoperative cholangitis. Other patients will not have ducts even when looked for microscopically. If this is indeed a dynamic situation, as Kasai's work seems to suggest, these patients not only will not be improved by the Kasai operation but they will be patients in whom the progressive extrahepatic biliary obstruction of the newborn has progressed too far to be amenable to surgical correction.

REFERENCES

1. Kasai, M.: Treatment of biliary atresia with special reference to hepatic portoenterostomy and its modifications. Progr. Ped. Surg., *6*:5, 1974.
2. Kasai, M., and Suzuki, S.: A new operation for "noncorrectable" biliary atresia; hepatic portoenterostomy. Shujutsu (Operation) *13*:733–739, 1959 (in Japanese).
3. Kasai, M., Asakura, Y., Suzuki, H., et al.: Modifications of hepatic portoenterostomy to prevent postoperative ascending cholangitis. Presented before the 5th Pacific Association of Pediatric Surgeons meeting, Tokyo, 1972.
4. Kimura, S.: Operation der angeborenen Gallengangsatresie-Hepatoportojejunostomie. Z. Kinderchir., *10*:60, 1971.
5. Koop, C. E.: Progressive extrahepatic biliary obstruction of the newborn. J. Ped. Surg., *10*:169, 1975.
6. Landing, B.: Changing approach to neonatal hepatitis and biliary atresia. Pediatrics, *53*:647, 1974.
7. Thaler, M. M., and Gellis, S. S.: Studies in neonatal hepatitis and biliary atresia. Am. J. Dis. Child., *116*:257–284, 1968.

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Imperforate Anus

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Analysis of imperforate anus is characterized by three important considerations: (1) the location of the "blind end" of the bowel; (2) the presence or absence of a fistula from the bowel; and (3) the course of any fistula and the structure to which it is connected. The classification of Ladd and Gross[8] was an important and useful contribution, but other classifications have been developed in order to indicate more completely the anatomy present in the affected child. These classifications tend to reflect the three considerations important to long-term results: (1) fecal continence; (2) a satisfactory genitourinary tract; and (3) a satisfactory position and function of the anus. In 1970, an international classification was suggested by an Ad Hoc Committee at the Pediatric Surgical Congress in Melbourne, Australia.[13] Table 1 gives our modification of this classification, which will serve as a guide to that which follows.

The major divisions of Table 1 are indicative of the level of the "blind end" of the rectum. Early authors[2, 9, 10] noted the relationship of functional result and mortality to the level of descent of the blind bowel. The levator sling is used in this classification to divide the anomalies into groups, with the blind bowel below, at the level of, or above the levator. Numerous studies[3, 4, 6, 11, 15, 19] have indicated the importance of the puborectalis component of the sling in regard to fecal continence.

Minor divisions of Table 1 take into consideration the degree of obstruction and type of fistula. Not included in this classification are the various complex genital tract anomalies which inevitably bear upon the surgical approach. These, as well as exstrophy, will be excluded from our discussion.

Figure 1 illustrates examples of the three basic types of deformity in the male. Figure 1*a* demonstrates the normal anatomy to be found in the male. A low (translevator) type is depicted in Figure 1*b*, with an anocutaneous fistula. The rectum can be seen to descend through the puborectalis and external sphincter muscles. The anus is not present in its normal location, but is rather anterior, connected by a fistulous tract.

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Table 1. *Classification of Anorectal Anomalies*

A. Low (Translevator)
- 1. At Normal Anal Site
  - a. Anal stenosis
  - b. Covered anus – complete
- 2. At Perineal Site
  - a. Anocutaneous fistula (covered anus – incomplete)
  - b. Anterior perineal anus
- 3. At Vulvar Site*

B. Intermediate
- 1. Anal Agenesis
  - a. Without fistula
  - b. With fistula
    - 1. Rectobulbar†
    - 2. Rectovestibular*
    - 3. Rectovaginal – low*
- 2. Anorectal Stenosis

C. High (Supralevator)
- 1. Anorectal Agenesis
  - a. Without fistula
  - b. With fistula
    - 1. Rectovesical
    - 2. Rectourethral†
    - 3. Rectovaginal–high*
    - 4. Rectocloacal
- 2. Rectal Atresia

D. Miscellaneous
- Imperforate anal membrane
- Cloacal exstrophy
- Others

*Females
†Males

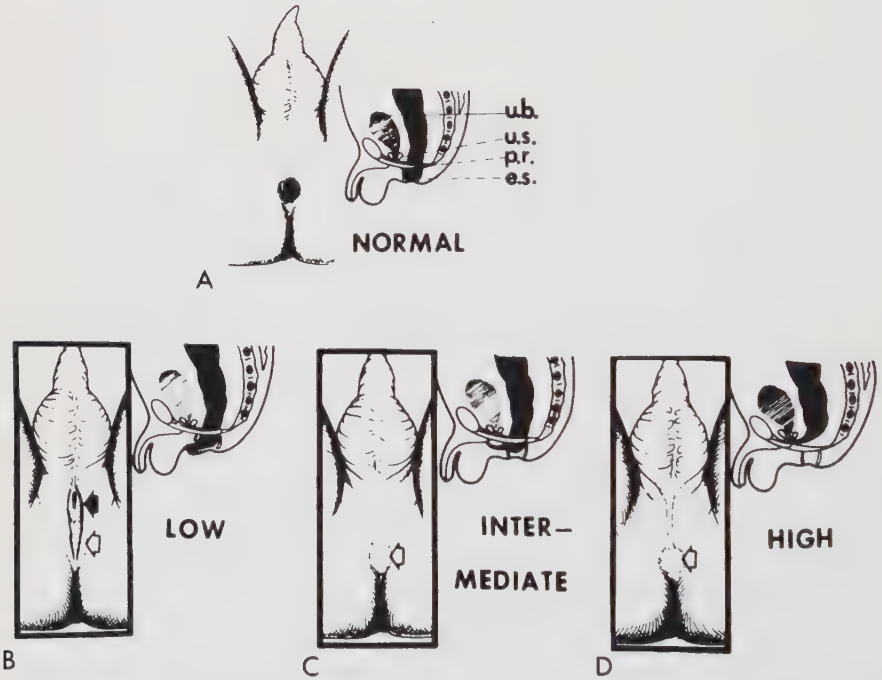

Figure 1. Examples of anorectal anomalies in the male: *u.b.* = urinary bladder; *u.s.* = urinary sphincter; *p.r.* = puborectalis muscle; *e.s.* = external anal sphincter. (Reproduced from Santulli, T. V.: Malformations of the anus and rectum. *In* Mustard, W. T., et al. (eds.): Pediatric Surgery. Chicago, Year Book Medical Publishers, Inc., 1969. Used with permission.)

Figure 1*c* illustrates an intermediate type, with the colon descending part or all the way through the puborectalis. The bowel ends blindly above the external sphincter, but a fistula empties into the urethral bulb. A high (supralevator) anomaly is shown in Figure 1*d*. The rectum ends above the puborectalis, with a fistula being present to the urethra below the urethral sphincter. Santulli et al.[8] and Stephens and Smith[18] give a more comprehensive classification and illustration of these anomalies in both male and female. Our condensation is done to simplify the classification and make possible a workable presentation of the diagnosis and treatment of this entity.

DIAGNOSIS

Proper treatment requires accurate determination of the child's anatomy. Establishment of the level of the blind bowel and presence or absence of fistulae must be done early. Although the baby is obstructed, urgency is no excuse for inaccuracy.

A meticulous physical examination of the baby should establish the baby's general condition, state of maturity, and the possibility of other anomalies. If inspection of the perineum discloses a bulging membrane or a bit of meconium, a valuable clue has been found. Meconium at any site other than the urethral meatus, vagina, or vestibule always signals a low type anomaly. These cutaneous fistulae occur in the midline. A line of small "epithelial pearls" running along the median raphe in the absence of meconium may also be indicative of a low type anomaly.

Except in the case of a straightforward anal stenosis, radiographic studies are recommended. The Wangensteen-Rice inversion x-ray[20] is of value. A period of 12 to 18 hours without gastric decompression is generally necessary for air to pass through the alimentary tract and into the low rectum. A small amount of barium paste is applied to the natal crease. The baby is held upside down for several minutes. The child is then positioned in front of the cassette, centering the greater trochanter. The hips should be flexed. The Roentgen tube should be at least 2 m from the cassette to avoid excessive magnification. Films are taken at 3 hourly intervals until no change in successive films is noted. A line drawn between the top of the pubis and the coccyx will define the pubococcygeal line and give a good idea of the relationship of the blind end to the puborectalis. If the blind end is within 1.5 to 2 cm of the barium marker, the anomaly is usually found to be of the translevator type. The presence of fistulae may allow air to escape and give a confusing picture. Crying may increase abdominal pressure and push the blind end deceptively low; caution must be used in the interpretation of such films. The use of radiopaque contrast material usually gives little more information than air contrast, and is of infrequent value in the work-up of the neonate. Direct needle aspiration of the rectal pouch can be very helpful in determining the level of the blind bowel if meconium is obtained; failure to obtain meconium is an equivocal finding. This will be elaborated upon below.

Because of the very high incidence of fistulae in the female, a careful inspection of the perineum, vestibule, and vagina will usually serve to define the level of the blind bowel. Bill et al.[1] emphasize the importance of the hymen in defining these lesions. The child with an obvious fistula to the perineum or posterior vestibule presents no problem, the lesion being of the translevator type. Children with meconium coming from high in the vagina are placed in the supralevator category. In the absence of an apparent external fistula, a normal appearing hymen indicates the presence of a translevator type, and a tiny fistulous opening should be found, perhaps hidden by a small flap of tissue in the posterior fourchette. If no hymen is present and, in particular, if no urethra is visible anteriorly, the lesion will probably be a high type with a rectovaginal or rectocloacal fistula.

Probing of a recto- or anovestibular fistula will disclose the direction and length of the fistulous tract and the probable level of the blind bowel. A common anovestibular fistula tends to guide the probe along the perineum, demonstrating the low level of the blind pouch. The rare rectovestibular fistula, on the other hand, runs in a direction parallel to the vagina, and attempts to push the probe in a direction parallel to the perineal skin are met with resistance.

Fistulae

The diagnostic value of the fistula has already been mentioned. However, successful management of imperforate anus depends upon proper treatment of rectourinary, rectovaginal, and rectocloacal fistulae. Santulli et al.[14] report a survey of over 1100 patients, in which 72 per cent of males and 90 per cent of females had fistulae. Twenty-five per cent of males had a high fistula to the urinary tract, and 33 per cent of females were noted to have rectocloacal, rectovaginal, or, rarely, rectovesical fistulae. The remainder of abnormal connections is associated with low, translevator lesions.

Failure to recognize a fistula at the time of definitive procedures will inevitably result in either operative damage to the urinary tract or persistence of the fistula. Such persistent rectourinary fistulae serve as a source for chronic, progressive urinary tract infection with loss of renal function. A persistent rectovaginal or rectocloacal fistula establishes the vagina as a cesspool which must be dealt with later. The difficulty of handling these fistulae in the neonatal period is such that the treatment may better be deferred to a later time, allowing the child to grow and simplifying surgical exposure and dissection.

ASSOCIATED ANOMALIES

Coincidental anomalies in other organ systems occur in from 25 to 75 per cent of children with imperforate anus. The higher figure reflects the frequency found in those series in which the babies are studied exhaustively for other anomalies. The babies with supralevator anomalies have more frequent and more severe associated anomalies. Some of

the anomalies by themselves are life-threatening and demand immediate treatment; in others, treatment may be safely postponed.

Skeletal and Neurologic

Skeletal anomalies constitute a large group of coexisting malformations. These range from relatively insignificant abnormalities, such as supernumerary digits, to massive derangements like agenesis of the sacrum and spina bifida. Their greatest importance lies in the neurologic deficits which frequently accompany the anomalies of the spine. Deficiencies in innervation of the pelvic musculature frequently occur with such lower spinal deformities, as well as alterations in muscular insertions. It is important, therefore, to obtain satisfactory anteroposterior and lateral views of the vertebral column in order to predict accurately the anatomy and function of the pelvic musculature.

As mentioned above, an assortment of other skeletal anomalies may be present, such as club feet or dislocated hips, which require specific treatment. We therefore emphasize again the importance of a thorough physical examination of the afflicted neonate.

Genitourinary

If we include the fistulous abnormalities, this system would be substantially the largest in terms of percentage of associated anomalies. Even excluding the fistulae, which are felt to represent part of the primary anorectal anomaly, patients will have as many associated abnormalities in this system as in the skeletal and nervous systems.

Double and septate vaginae, as well as bicornuate and double uteri, constitute the most frequently encountered genital anomalies.

Smith,[17] Wiener and Kiesewetter,[21] and Singh et al.[16] have recently reported separate series of patients with urologic abnormalities and imperforate anus. Table 2 gives the results of this collective series of 370 patients. Bilateral renal agenesis or bilateral dysplasia (either alone or in association with the triad syndrome) may be incompatible with life and are resistant to any treatment. However, several of the abnormalities

Table 2. *Urologic Anomalies with Imperforate Anus*

	MELBOURNE[1]	PITTSBURGH[16]	SHEFFIELD[7]	COMBINED
Total cases reported	57	200	113	370
Bilateral renal agenesis	1	5		6
Solitary kidney	3	15	11	29
Hypoplastic kidney	5	4		9
Renal dysplasia		6	4	10
Triad syndrome	2	2		4
Obstruction (U–P, U–V)		10		10
Hydronephrosis (unspecified)	4			4
Ureteral reflux	13	11		24
Bladder urethral diverticula	2	2	1	5
Urethral stricture or valves	2	2		5
Hypospadias, epispadias	12	13		25
Miscellaneous	4	16		20

require prompt specific treatment in order to avoid deterioration of already impaired renal function. Neurogenic bladder may be the source of recurring infection. Careful neurologic examination of the neonate's sacrococcygeal nerve segments will alert the physician to this possibility. Urinary diversion may ultimately be required.

The continuing surveillance for urologic problems begins in the neonatal period. An intravenous urogram is performed in all patients during the first hospitalization. An attempt to obtain a voiding phase of this study is made, realizing that it is frequently unsatisfactory. Cystograms are performed at a later time in those patients with high lesions. Periodic urine culture and intravenous urography are performed when indicated. Cystoscopy may be of real value in determining the level of a urinary fistula or in the demonstration of a postoperative diverticulum or stricture. This diligence, coupled with appropriate investigative studies, should identify serious abnormalities of the urinary tract before extensive renal deterioration occurs. Appropriate corrective surgery or suppressive antibiotics can then be instituted to avoid further loss of kidney function due to obstruction or infection.

Alimentary Tract

Ten per cent of children with imperforate anus will have esophageal atresia with or without tracheoesophageal fistula.[7] One of the first maneuvers to be performed in the neonate with imperforate anus, therefore, is to pass a nasogastric tube into the stomach. Obstruction of the esophagus due to atresia will prevent passage of the tube beyond the cervical area, and a chest film will demonstrate the tube to be curled in the proximal pouch. Treatment of this anomaly will take precedence over treatment of the anorectal anomaly initially.

Atresias of the small and large intestine can coexist with imperforate anus, greatly confusing the picture. If the inversion x-ray fails to demonstrate gas in the rectum or distal colon after 24 to 36 hours, serious consideration must be given to the presence of a proximal atresia. This, of course, will require an exploratory procedure for the atresia. Except in the simplest anorectal anomalies, a colostomy should probably be done in these cases in order to avoid anastomotic complications.

Cardiovascular

Cyanosis, murmurs, or cardiac failure may indicate the presence of an associated cardiac anomaly. Treatment of these can generally be postponed, although a child with cardiac failure or severe cyanosis may require an emergency operation within the first few days. Antibiotic coverage during gastrointestinal or urologic procedures is important to avoid bacterial endocarditis.

TREATMENT

Within the first 24 to 36 hours, the surgeon should have completed his initial evaluation of the child. Coexisting problems and anomalies

should generally have been diagnosed and should be under control. The level of the blind bowel should have been determined by means of physical examination, radiography, or needle aspiration. Uncertainty, if it exists, should be between relatively narrow limits. If major uncertainties still exist, regarding either the level of the blind bowel or presence of a fistula, the only safe approach at this point is establishment of a colostomy. We shall discuss the treatment of these anomalies according to their classification (see Table 1).

Translevator Anomalies

Anal stenosis can be satisfactorily handled in the neonate by simple dilation using Hegar dilators. The anus is gradually enlarged to a size sufficient to allow daily dilation by the mother using her little finger. The same technique can be used in those anocutaneous fistulae in which a short fistula passes through the external sphincter. Most anovulvar fistulae can also be handled in the neonate by simple dilations. One is often gratified to observe that, as the child grows and the perineal body develops, the anus moves posteriorly and leaves a satisfactory distance between vulva and anus. Cases with an imperforate anal membrane can be handled similarly after the membrane is punctured using a hemostat or scalpel.

Cases of covered anus or low pouch without fistula are handled by an anoplasty of the type depicted in Figure 2. A cruciate incision is made over the external sphincter and careful dissection up to the rectal pouch allows it to be incised in a similar cruciate fashion. The flaps are interposed, accurately suturing mucosa to skin. No dilations are done for the first 10 days although gentle irrigations, using a small soft rub-

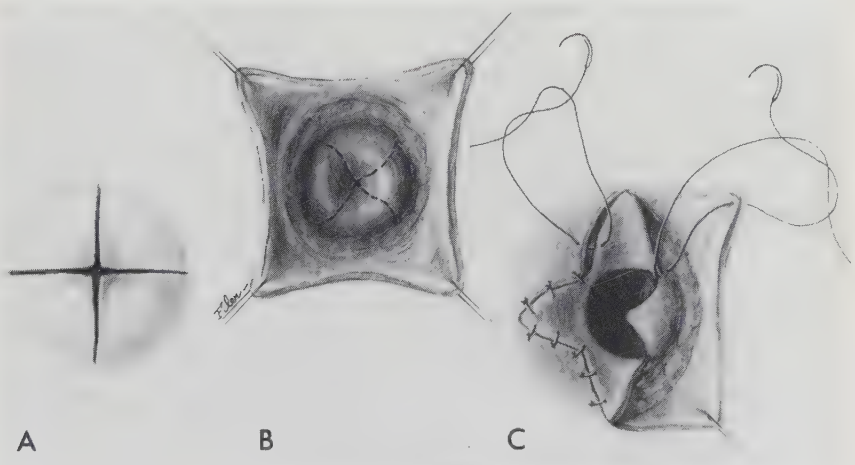

Figure 2. Anoplasty for covered anus without fistula: *a*, cruciate skin incision centered over external sphincter; *b*, skin flaps elevated. Blind bowel with proposed incision seen in depth; *c*, construction of anastomosis.

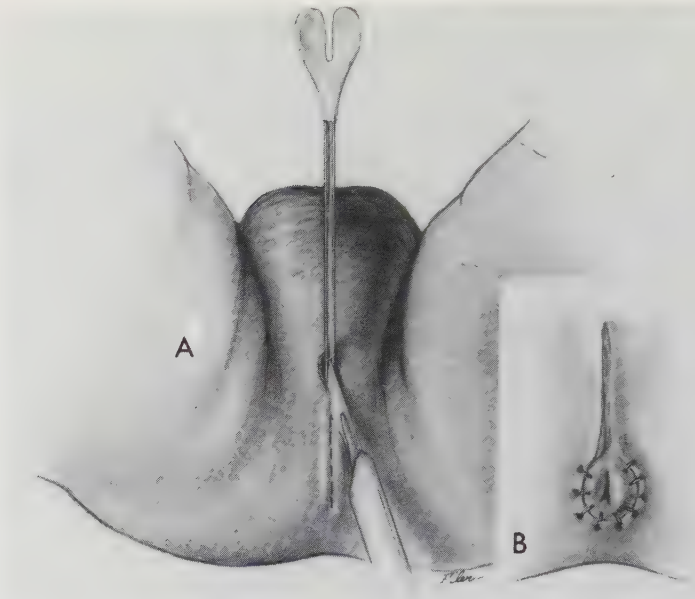

Figure 3. Anoplasty for covered anus with cutaneous fistula. *a*, The fistulous tract has been dilated and a grooved director inserted. The fistula is incised as shown or with scissors. *b*, The rectal mucosa has been sutured to the skin. The epithelium along the tract anteriorly will be scraped away.

ber catheter, will be of help with stooling. Dilations will then be instituted and taught to the mother.

In males, the fistula is often too long for dilation alone, and an anoplasty is quite satisfactorily applied to this problem. Figure 3 illustrates this type of anoplasty. On occasion, these fistulae are extremely difficult to find, only the slightest tinge of green, gray, or black being apparent. When the fistulous opening is found, it is gradually dilated, beginning with filiforms and proceeding to a size which will allow one blade of a scissor to be passed into it. At times, insertion of a catheter is helpful. The fistula is opened all the way to the external sphincter, where the mucosa is identified and carefully sutured to skin, after excision of redundant overlying tissue. The tract of the fistula is then scraped with a knife blade to remove the ectopic epithelium. Dilations are begun after 10 days.

The female with rectovestibular fistula can be handled in the neonatal period, using simple dilations, although, in these girls, the perineal body will generally not develop sufficiently for the genital area to remain clean. In addition, dilations tear in an anterior direction, accentuating the problem. Figure 4 depicts a "cut-back" procedure in general use, which facilitates enlargement of the fistula in a posterior direction only, preserving any space between the fistula and the vagina. A formal transplant of the fistula posteriorly has been favored by many authors, although we agree with Stephens and Smith,[18] who reserve transplanta-

Figure 4. Cutback for translevator anomaly with anovestibular fistula. The scissor has been inserted into the rectum through the fistula. The proposed incision is marked.

tion for those patients in whom, later on, genital soiling constitutes a hygienic or social problem.

Intermediate Anomalies

Males with rectourinary fistulae and females with rectovaginal fistulae should undergo colostomy as neonates. The length of some anorectal stenoses will not allow satisfactory dilation for proper bowel function, and these will also require colostomy. However, in these patients with stenoses, if dilations are effective, the child has been spared a complicated operation. The technique of the colostomy will be described below. When the distal end of the blind pouch resides just below the pubococcygeal line by invertogram, the experienced surgeon may legitimately attempt exploration from below. If needle aspiration does not yield meconium within 1.5 cm, and unless a fistula has been ruled out, good judgment requires colostomy and exploration later.

Perineal exploration in the newborn must be done with great caution. An attempt to perform a pull-through procedure of a high or questionable intermediate lesion in the neonatal period must be condemned because of generally poor results. The delicate musculature responsible for continence is too easily damaged at this early age. Therefore, perineal exploration is reserved for translevator and low intermediate lesions. Accuracy in determining the level of the bowel is thus of primary importance in deciding whether or not a colostomy should be done in the neonatal period.

Supralevator Anomalies

These anomalies are all handled by neonatal colostomy and pull-through at a later date. Even the most experienced surgeon can scarcely avoid damage to the delicate pelvic musculature and nerves of the neonate.

THE COLOSTOMY. The position and technique of the colostomy are points of minor controversy. Some surgeons favor the sigmoid end colostomy because of its easier performance and lack of fecal contamination of urinary fistulae. However, this colostomy inevitably compromises the blind pouch and may cause injury to the urinary tract because of traction upon a fistula. We use the rectal pouch in the definitive repair, and for that reason this type of colostomy is not desirable. We favor a left transverse divided colostomy. Its position allows the subsequent pull-through procedure to be performed without the need to move, close, or manipulate the contaminated stoma. Because of the skin bridge between the loops, fecal contamination of the distal segment and urinary fistulae is minimized. Our technique follows.

During the 24 hours or so required for establishment of the level of the blind bowel, the child is evaluated as described previously. An intravenous catheter has been placed, and the baby has received 1 mg of Aquamephyton. Nasogastric suction has been instituted before abdominal distention becomes pronounced. The baby's entire abdomen is prepared and draped. A right upper quadrant incision, about 4 cm long, is made and carried down through the peritoneum, splitting the muscles. The distended transverse colon is easy to find and is brought up gently into the wound. The mesentery is incised and the bowel divided between clamps. A suction catheter is used to remove meconium as the clamp is released. The distal loop is irrigated with copious quantities of saline and as much meconium as possible is removed. This is done to prevent inspissation and urinary tract infection. The proximal loop is sutured to the one end of the wound, the distal loop to the other. Fine silk is used to suture the bowel to each layer, giving a 1 to 1½ cm bridge of fascia and skin between the loops. The stoma is matured primarily using submucosa-to-subcuticulum sutures of fine chromic. The distal stoma is made as small as possible to avoid prolapse.

Postoperative care includes cautious advancement of feeding and stomal skin care. An intravenous urogram, if not already obtained, is done before discharge. A contrast study of the distal colonic loop can be done using thin barium, if desired, although this may be postponed and performed later.

THE SACROABDOMINOPERINEAL APPROACH. Definitive therapy for the high supralevator type anomalies is best undertaken between the ages of 6 and 12 months. At this time, the structures are large enough to be well identified and utilized. We prefer the sacroabdominoperineal pull-through procedure for all supralevator lesions that have no fistula or are associated with high rectovaginal or rectourinary fistulae (both rectourethral and rectovesical). We believe this combined approach allows for a direct visualization of the all-important levator sling and future puborectalis component, so as to be certain that the pull-through is

within these structures and thereby provides maximal expectations of continence.

The pull-through procedure consists of a sacral and an abdominal portion.[5] The sacral approach is used to localize the puborectalis muscle and to prepare the channel for subsequent pull-through of the rectosigmoid to the outside. The patient is placed in a face-down position, a metal urethral sound having been inserted. The incision is made slightly below the tip of the coccyx in a transverse manner, and dissection is carried down in the midline until one encounters the urethra with its inserted sound. Careful approach towards the coccyx will then reveal the horseshoe-shaped puborectalis muscle closely adherent to the urethra. It can be separated judiciously, and a series of Hegar dilators utilized to make a channel for the future pull-through. A cruciate incision is made over the external sphincter and this muscle divided at 12 and 6 o'clock, in order to embrace the pulled-through rectosigmoid. A 1 inch Penrose drain is inserted through the external sphincter and up underneath the puborectalis muscle as a point of future reference and identification of the pull-through channel. The completed sacral approach before closure is portrayed in Figure 5.

The abdominal portion of the operation is then carried out after the sacral incision has been closed in standard fashion and the child turned over. After a conventional abdominal incision, a point approximately 6 to 10 cm above the end of the blind bowel is chosen for transection. In-

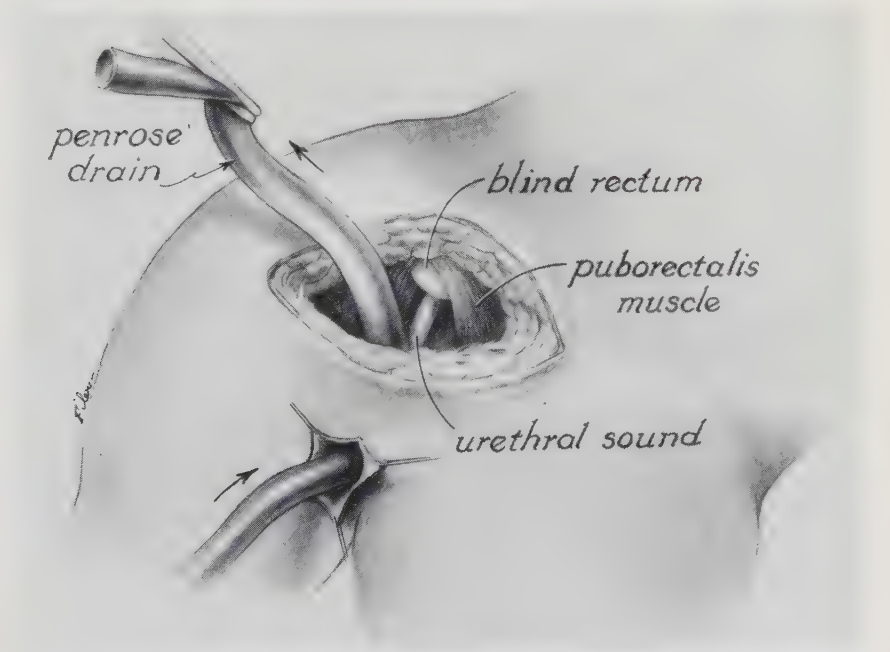

Figure 5. The sacral portion of the pull-through procedure showing the puborectalis muscle, blind bowel, and urethra. A Penrose drain is shown brought in through the external sphincter area within the projected pull-through channel.

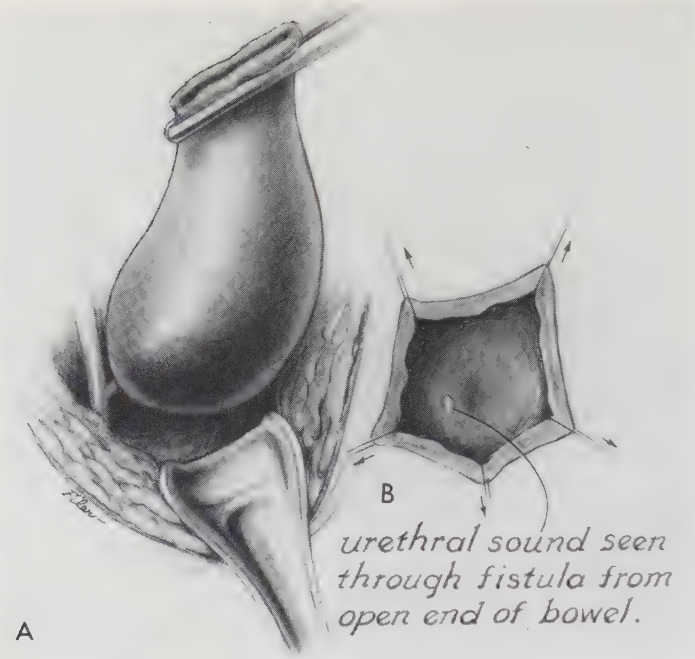

Figure 6. *a*, The blind rectum showing a rectourinary fistula. *b*, The view inside the seromuscular cuff of blind bowel after the mucosa has been removed and the fistula oversewn with a protective urethral sound in place.

jection of saline in the seromuscular coat and a vertical incision about 3 cm in length will enable one to separate the seromuscular cuff from the underlying mucosa all the way around the circumference of the bowel. The mucosa is then double clamped and divided, with the seromuscular cuff transected as well. The mucosa is cored out, as seen in Figure 6, from the seromuscular cuff down to where the fistula to the vagina or urinary tract comes off. This fistula is transfixed with catgut and the extra mucosa removed. A Hegar dilator is then inserted within the previously placed Penrose sheath drain until one can see it indent the bottom of the seromuscular cuff, as shown in Figure 7. An incision is made on the Hegar dilator and an opening made in the seromuscular cuff, through which the Penrose sheath drain can be brought into the field. The previously mobilized rectosigmoid is then drawn through the opening in the seromuscular cuff, using the Penrose sheath drain as a guide. The drain should not be used for traction but simply as a guide. Long Kelly or Allis clamps have to be passed through the puborectalis channel and into the seromuscular cuff to grasp the bowel that is to be pulled through. Once the bowel is pulled in the correct channel to the outside, the cruciate skin incisions are interdigitated with the full thickness of the pull-through bowel, so as to lessen the chance of cicatricial contraction. The seromuscular cuff is sewed to the pull-through segment with a few loose sutures after drainage per abdominal stab wound. Routine closure of the abdomen follows.

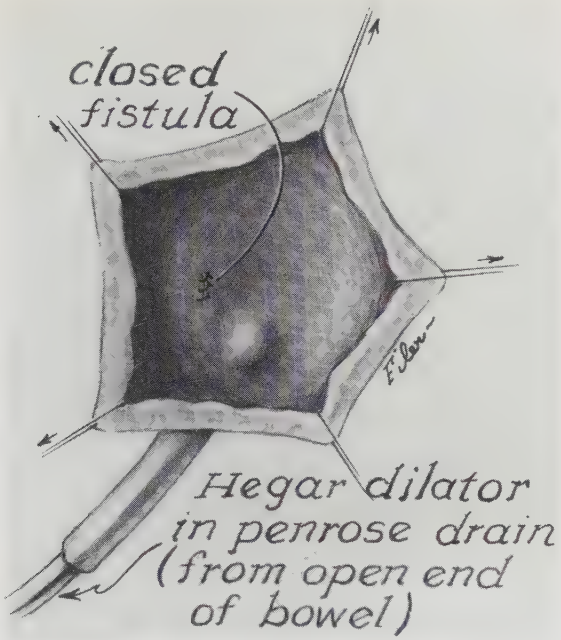

Figure 7. A Hegar dilator has been passed through the inside of the Penrose drain and is indenting the blind bowel seromuscular cuff. This is the point at which the cuff is opened and the proximal colon pulled through.

Postoperative care consists of dilating the new anus judiciously in approximately 7 days.

This same abdominal portion of the procedure can be used for low, translevator lesions that have fistulas to the urinary tract (which occurs rarely). The stripping of the mucosa from the abdominal side without a sacral incision will often suffice, because the bowel has already traversed the puborectalis muscle and can be very readily joined to a perineal incision without direct sacral visualization.

RESULTS

Mortality

Imperforate anus carries an irreducible inherent mortality because of the associated anomalies that so often go with it. We have recently reviewed a series of 284 cases of imperforate anus and found the raw, overall mortality to be 58 patients (20 per cent). As might be expected, the greater mortality rates occurred in the more complicated intermediate and supralevator lesions (Table 3). The intermediate lesion had the highest loss of all, with 10 deaths in 22 patients (45 per cent); all of these deaths were from major associated congenital anomalies.

It is of interest to note that, on further examination of the causes of

Table 3. *Mortality Associated with Repair of Imperforate Anus*

LESION	TOTAL	DEATHS
Translevator	128	9 (7 per cent)
Intermediate	22	10 (45 per cent)
Supralevator	134	39 (29 per cent)
Overall	284	58 (20 per cent)

death in the 58 patients who succumbed, there were only seven in whom death could be directly or inferentially the result of imperforate anus itself. There were four patients who had an uncertain cause of death because they died outside of the hospital, leaving 47 patients (81 per cent) whose mortality could rightfully be attributed to causes unrelated to imperforate anus. In a high percentage of these 47, the death was due to associated congenital anomalies such as congenital heart disease, mongolism, septicemia in a premature infant, esophageal atresia, and severe genitourinary or central nervous system problems.

Continence

Not only is it of importance to know how many patients survive having an imperforate anus, but the quality of life and continence achieved by these children as they grow up must be assessed. The same group of 284 patients mentioned above have been followed from a continence standpoint; we have eliminated those who succumbed, those with mental retardation, and those with no definitive therapy for their imperforate anus except a permanent colostomy. There were only three of the latter. We were able to assess accurately the state of continence in 84 per cent of the remaining 226 patients (Table 4). The follow-up period ranged from 5 to 30 years. Twelve per cent of them had what would be judged a frankly poor result. Such a child was rarely continent or had a permanent colostomy because definitive therapy had failed. Not surprisingly, 21 of these 23 poor results occurred in intermediate and supralevator types who were not only the most numerous, but also had the most difficult problems to deal with. The supralevator type alone accounted for 19 out of 23 poor results in the entire series. This left us with 168 out of 191 patients (88 per cent) followed who could be classified as having good or fair results. Seventy-four per cent of the total series pre-

Table 4. *Continence Following Repair of Imperforate Anus*

LESION	GOOD	FAIR	POOR
Translevator	89	6	2
Intermediate	10	0	2
Supralevator	42	21	19
Overall	141 (74 per cent)	27 (14 per cent)	23 (12 per cent)

sented with good results in which the patient had satisfactory ability to control defecation and to lead a normal life, with the possible exception of some temporary difficulty when diarrhea occurred or under physical stress. Fourteen per cent of the patients had fair results. By our definition, this means that the patient had socially acceptable continence most of the time, but did have occasional soiling or staining accidents.

It must be pointed out that some of the good results were in patients who, by various stratagems, had been able to control a situation in which their anatomy would not be considered adequate for continence. Such adaptations included careful avoidance of laxative foods and willingness to allow constipation to occur with a bowel movement pattern set up for every third or fourth day. These were classified as good results because of the functional continence that had been achieved, rather than the anatomy the patient had.

It is of interest, also, to note that a number of the poor results had explanations that did not suggest surgical failure; they included such things as severe psychological problems on the part of the patient, or poor home environment which resulted in lack of motivation to continence.

Finally, it should be noted that, with the passage of time, the degree of continence became greater in most patients. It was rarely due to any change in the anatomy that the child was working with, but resulted from his desire to maximally use that which he had. This change in outlook most often occurred after the age of 10, as the child began to go through puberty; it then was not socially acceptable to soil one's self or to have an odor. We noted that about a quarter of the good and fair results went through a distinct evolutionary process in which they upgraded their degree of continence as they advanced in age.

SUMMARY

Successful treatment of the child with imperforate anus yields an individual with satisfactory continence and a healthy urinary tract. These goals are achieved by accurate evaluation of the newborn, optimal technical results, and conscientious follow-up. The infant born with one of these malformations frequently has a serious associated anomaly which also requires early specific diagnosis and management.

When the bowel has passed through the puborectalis in utero, the deformity can often be definitively treated in the neonate by dilations or anoplasty. However, if a urinary or high vaginal fistula is present, or if the anomaly is of the supralevator type, definitive surgery is best postponed some months and the neonate given a colostomy. We have found the sacroabdominoperitoneal approach to be the most satisfactory pull-through procedure for the supralevator lesion.

The children with high, supralevator anomalies have higher mortality rates and, in one out of four cases, have suboptimal fecal continence. They require the utmost in technical skill and continuing care if they are to live full lives free of social stigma. The mortality rate in all other types is low and the functional continence uniformly acceptable.

REFERENCES

1. Bill, A. H., Hall, D. G., and Johnson, R. J.: Position of rectal fistula in relation to the hymen in 46 girls with imperforate anus. J. Ped. Surg., *10*:361, 1975.
2. Cule, J. H.: John Pughe, 1814–1974. Ann. Roy. Coll. Surg. Eng., 37 247, 1965.
3. Karkowsky, J., Pollack, W. F., and Landon, C. W.: Imperforate anus: An 18–30 year follow-up study. Am. J. Surg., *126*:141, 1963.
4. Kiesewetter, W. B.: Imperforate anus: The rationale and results of the sacroabdominoperineal operation. Ann. Surg., *164*:655, 1966.
5. Kiesewetter, W. B.: Imperforate anus II—The rationale and technique of the sacroabdominoperineal operation. J. Ped. Surg., 2:106, 1967.
6. Kiesewetter, W. B., and Nixon, H. H.: Imperforate anus I—Its surgical anatomy. J. Ped. Surg., 2:60, 1967.
7. Kiesewetter, W. B., Turner, C. R., and Sieber, W. K.: Imperforate anus: Review of a 16 year experience with 146 patients. Am. J. Surg., *107*:412, 1964.
8. Ladd, W. E., and Gross, R. E.: Congenital malformations of the anus and rectum: Report of 162 cases. Am. J. Surg., 23:167, 1934.
9. Mastin, W. M.: A resume of the surgical treatment of anorectal imperforation in the newborn. Surg. Gynec. Obstet., 7:316, 1908.
10. Matas, R.: The surgical treatment of congenital ano-rectal imperforation considered in the light of modern operative procedures. Tr. Am. Surg., *15*:453, 1897.
11. Nixon, H. H.: Imperforate Anus: British Surgical Practice and Surgical Progress. London, Butterworths, 1961.
12. Potts, W. J.: The Surgeon and the Child. Philadelphia, W. B. Saunders Co., 1959.
13. Santulli, T. V., Kiesewetter, W. B., and Bill, A. H., Jr.: Anorectal anomalies: A suggested international classification. J. Ped. Surg., 5:281, 1970.
14. Santulli, T. V., Schullinger, J. N., Kiesewetter, W. B., and Bill, A. H., Jr.: Imperforate anus: A survey from the members of the surgical section of the American Academy of Pediatrics. J. Ped. Surg., *6*:484, 1971.
15. Scharli, A. F., and Kiesewetter, W. B.: Imperforate anus: Anal rectal sigmoid pressure studies as a quantitative evaluation of postoperative continence. J. Ped. Surg., *4*:694, 1969.
16. Singh, M. P., Haddadin, A., Zachary, R. B., and Pilling, D. W.: Renal tract disease in imperforate anus. J. Ped. Surg., *9*:197, 1974.
17. Smith, E. D.: Urinary anomalies and complications in imperforate anus and rectum. J. Ped. Surg., *3*:337, 1968.
18. Stephens, F. D., and Smith, E. D.: Anorectal Malformations in Children. Chicago, Yearbook Medical Publishers, Inc., 1961.
19. Taylor, I., Duthie, H. L., and Zachary, R. B.: Anal continence following surgery for imperforate anus. J. Ped. Surg., *8*:497, 1973.
20. Wangensteen, O. H., and Rice, C. O.: Imperforate anus, a method of determining the surgical approach. Surgery, 92:77, 1930.
21. Wiener, E. S., and Kiesewetter, W. B.: Urologic abnormalities associated with imperforate anus. J. Ped. Surg., *8*:151, 1973.

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Total Parenteral Nutrition in Infants and Children: Central and Peripheral Approaches

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Insufficient caloric intake for a prolonged period contributes appreciably to mortality in infants and children with lesions of the gastrointestinal tract. Not uncommonly, patients with persistent intestinal obstruction, bowel fistulas, or short-bowel syndrome die solely of inanition and its complications before curative treatment or appropriate surgical procedures can be carried out.

Dudrick and co-workers[8, 9] first demonstrated that the intravenous infusion of a fat-free, amino acid, glucose solution could support normal growth and development. Filler and co-workers[11] reported the successful long-term use of this solution in 14 critically ill infants with a variety of gastrointestinal disorders. Our experience since then and reports from other institutions indicate the lifesaving potential of total parenteral nutrition (TPN) in infants and children with inadequate gastrointestinal tract function.

Success of this mode of treatment was brought about by the development of special techniques for the intravenous administration of adequate quantities of calories and nitrogen. Use of this life-sustaining system requires the careful selection of patients for therapy, constant surveillance for complications, and attention to the minute details of procedures which minimize these dangers.

In recent years, an alternative approach to hyperalimentation in infants and children has been adopted in the United States and abroad. This technique involves the infusion of fat solutions along with glucose and amino acids into peripheral veins.[2-5] This program obviates the need for a central venous catheter, thereby eliminating certain complications. Because of the commercial unavailability of intravenous fat solutions in the United States, peripheral hyperalimentation without lipid emulsions

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has more recently been utilized in a number of institutions.[12] In many clinical situations the choice of one technique over the others involves individual patient consideration.

INDICATIONS

Central hyperalimentation has been used extensively at the Children's Hospital Medical Center since 1968. To date more than 250 infants and children have been treated. During the 2½ year period from January, 1972 to June, 1974, 80 infants and children at the Los Angeles County–USC Medical Center and Los Angeles Children's Hospital received intravenous feeding through peripheral veins using the fat emulsion Intralipid.* In addition, from July, 1974 to July, 1975, over 30 infants and children at the Mott Children's Hospital in the University of Michigan Medical Center were treated with peripheral hyperalimentation composed of fat-free solutions.

TPN is reserved for those infants and children whose lives are threatened because feeding by means of the gastrointestinal tract is impossible, inadequate, or hazardous. The goal of treatment depends on the patient's underlying condition. In some instances, such as in those infants with chronic nonspecific diarrhea, placing the gastrointestinal tract at rest for a prolonged period is curative. In others, the restoration and maintenance of adequate nutrition will permit correctible surgery.

The common conditions for which this treatment has been used include chronic intestinal obstruction due to adhesions or peritoneal sepsis, bowel fistulas, inadequate intestinal length, chronic severe diarrhea, extensive body burns, and abdominal tumors treated by surgery, irradiation, and chemotherapy. Although TPN is used to replete the malnourished child, it may be started prophylactically in clinical situations where prolonged starvation is expected.

As confidence and experience with the method have grown, additional indications for its use have developed. For example, with certain modifications, we have employed TPN in very small premature infants (less than 1 kg) who, despite an apparently normal gastrointestinal tract, constantly regurgitate feedings placed in the stomach either by gavage or by gastrostomy. Dudrick and others[7] have successfully treated uremia and hyperkalemia of acute renal failure with intravenous infusions of purified amino acids and glucose, thus reducing the need for dialysis.

The decision to begin a program of total intravenous alimentation requires mature clinical judgment. Such a decision can be made readily for an infant with complicated omphalocele or for one in whom a large portion of the midgut has been resected because of volvulus. In others, the decision may be more difficult. For example, in a child with chronic diarrhea and malnutrition, one must be certain that customary therapy has failed before beginning total intravenous therapy. Although anorexia, vomiting, and diarrhea commonly accompany irradiation and

*Manufactured by Vitrum Company, Stockholm, Sweden and kindly supplied by Cutter Laboratories, Berkeley, California.

chemotherapy, only the occasional patient becomes so debilitated that treatment is required.

One must weigh the need for improved nutrition to save life and reduce morbidity against the possibility of serious complications, especially sepsis. TPN should not be employed in those children in whom nutrients can be safely delivered and absorbed from the gastrointestinal tract by oral feedings, gavage, or gastrostomy. On the other hand, our experience indicates that when the technique is applied with proper care, the threat of serious morbidity is sufficiently low to justify its use in an ever increasing number of patients.

COMPOSITION OF SOLUTIONS

The composition of the two basic solutions for TPN used at Children's Hospital Medical Center is noted in Table I. Solution No. 1 (1000 ml) is infused daily and supplies an appropriate mixture of calories, nutrients, fluid, vitamins, and minerals for all patients. In larger patients, the use of more than 1000 ml Solution No. 1 will result in the infusion of excessive quantities of calcium, vitamin A and D, and trace metals. Therefore, after 1000 ml of Solution No. 1 is infused in a day, Solution No. 2 is given for any additional requirements.

Half-strength solutions (basic formula diluted in half with 5 per cent dextrose in water) are also prepared by the pharmacy and are used primarily during the first day or two of therapy. During this period, the child is adapting to the very high glucose load and the high concentration of glucose may produce an osmotic diuresis which will lead to hypertonic dehydration. As the patient's tolerance develops, as judged from diminishing glycosuria, full-strength solutions may be used. The administration of insulin is not necessary for nondiabetic children.

In most patients, additional sodium, potassium, and chloride are necessary. Usually the addition of 30 mEq of NaCl and 20 mEq KCl to the standard infusate will suffice and will not overburden the normal infant's kidney or cardiovascular system. The electrolyte content of different amino acid sources vary, a factor which must be considered if an amino acid preparation other than that listed in Table 1 is used. Children with normal renal function rarely have serum electrolyte abnormalities with this program. However, more caution is necessary for those with reduced renal function and other metabolic defects.

Iron requirements are met either by weekly intramuscular injections of iron dextran or by blood transfusion. When calculating the iron dose, one must remember that the intravenous dose need only be $^1/_{10}$ to $^1/_5$ the oral dose. Trace metals are now added to the basic mixture routinely (see Table 1).

PERIPHERAL FEEDING WITH FAT

The infusate consists of two separate bottles; one bottle contains only the fat emulsion, Intralipid, and the other bottle contains the amino

Table 1. *Contents of Central Infusate (Hyprotigen*-Dextrose)*

CONSTITUENT	CONTENT PER LITER
Protein hydrolysate	30.0 gm
Dextrose (hydrous)	196.6 gm
Sodium†	15.0 mEq
Potassium†	16.0 mEq
Calcium	27.0 mEq
Phosphorus	19.0 mEq
Magnesium	7.6 mEq
Chloride†	10.8 mEq
Folic acid	0.5 mg
Multivitamin infusion‡	5.0 ml
Vitamin K_1	0.2 mg
Vitamin B_{12}	6.6 μg

*Casein hydrolysate, McGaw Laboratories.

†Further adjusted at bedside.

‡U.S. Vitamin and Pharmaceutical Corporation. Each liter provides 4.8 gm nitrogen and 800 cal.

acids, glucose, electrolytes, and vitamins. Tables 2 and 3 list the infusate contents for infants and children, respectively. The dosage schedule listed in Table 2 is for infants up to 1 year of age. In patients older than 1 year, the program in Table 3 is utilized. The total number of calories administered can be increased by infusion of more fat (up to 5 gm

Table 2. *Protocol for the Peripheral Intravenous Feeding of Infants with Fat*

CONSTITUENT	VOLUME (ml per kg body wt per 24 hr)	AMOUNT (gm per kg body wt per 24 hr)	CALORIES
10 per cent Intralipid	40	4	44
5 per cent Amigen* in 5 per cent glucose	80	4 (protein)	32
10 per cent glucose	30	3	12
Total volume	150		
Total calories			88

Electrolyte and Vitamin Contents per Liter

Sodium	43.0
Potassium	46.0
Calcium	10.5
Magnesium	6.0
Chloride	67.0
Phosphate	29.0
Multivitamin Infusion (MVI)†	1.7 ml
Folic acid	1.5 mg
Aqua Mephyton	1.0 mg
Vitamin B_{12}	10.0 μg

*Manufactured by McGaw Laboratories, Glendale, California. The crystalline amino acid solution, Fre-Amine, can be used instead of the protein hydrolysate, Amigen.

†U.S. Vitamin and Pharmaceutical Corporation, New York, New York.

Table 3. *Protocol for the Peripheral Intravenous Feeding of Children with Fat*

CONSTITUENT	VOLUME (ml per kg body wt per 24 hr)	AMOUNT (gm per kg body wt per 24 hr)	CALORIES
10 per cent Intralipid	30	3	33
5 per cent Amigen in 5 per cent glucose	40	2 (protein)	16
10 per cent glucose	30	3	12
Total volume	100		
Total calories			61

per kg per day) and/or more 10 per cent glucose. The bottle containing the amino acids is prepared aseptically under a laminar flow hood in the hospital pharmacy. Essential fatty acids are present in the Intralipid in large quantities.

PERIPHERAL FEEDING WITHOUT FAT

A stock solution of 10 per cent Amigen* is used to make up the infusate. The mixing is carried out in the hospital pharmacy under a laminar flow hood. The amino acid solution is diluted with glucose to make up a 2 per cent protein hydrolysate in a 12 per cent glucose solution. The final solution contains 0.56 cal per ml. Electrolytes are added to the infusate to provide the recommended daily requirements plus additional needs based on the patient's clinical condition (Table 4). The electrolyte and vitamin concentrations are essentially the same as those recommended for central feeding and peripheral feeding with fat. Heparin at 0.5 units per ml is added to the solution to reduce phlebitis. In

*Manufactured by McGaw Laboratories, Glendale, California.

Table 4. *Peripheral Hyperalimentation without Fat*

CONSTITUENT	AMOUNT PER KG PER 24 HR
Water	200 to 250 ml
Protein	4 to 5 gm
Glucose	24 to 30 gm
Calories	112 to 140
Heparin	100 I.U.*
Sodium	2 to 4 mEq
Potassium	2 to 3 mEq
Chloride	2 to 4 mEq
Magnesium	0.6 mEq
Calcium	1.0 mEq
Phosphate	3.5 mm

International Units.

addition, the major portion of the essential fatty acids needed is supplied through the application of sunflower-seed oil to the skin of the infant's chest daily.[18] For both peripheral venous methods of feeding, the administration of iron is as described in the central feeding program. Trace metals are given as necessary.

METHODS

Central Feeding

Hypertonic infusates must be delivered through a central venous catheter to avoid peripheral venous inflammation and thrombosis. For this purpose, a silicone rubber catheter is passed through the internal or external jugular vein to the superior vena cava. This procedure is best carried out in an operating room or cardiac catheterization laboratory where adequate exposure, proper instruments, and strict aseptic conditions are available. To minimize bloodstream contamination, the venous catheter is tunneled from the vein entry point to a skin exit site which is placed 2 to 4 inches away. In the infant, it is brought out on the scalp, whereas in the older child, the exit site may be the neck or upper extremity. Central venous intubation by percutaneous subclavian vein puncture has also been used. The silicone rubber venous line may be left in place until the completion of therapy unless it becomes accidentally dislodged or septic complications develop. We have had a single catheter in place for as long as 120 days.

The central venous catheter can be inserted under local or general anesthesia. The head is turned to the side and the scalp carefully shaved. A transverse incision, 1 to 2 cm long, is made over the sternocleidomastoid muscle at the junction of the middle and lower third of the neck. The external or internal jugular vein is prepared for cannulation. The external jugular vein is ordinarily preferred and can usually be successfully cannulated even in the premature infant. However, if either external jugular vein is unavailable because of previous use or small caliber, or if entrance of the catheter from the external jugular vein into the vena cava is not possible, the internal jugular vein can be used for cannulation. A long hollow needle with an obturator in place is passed beneath the skin of the neck from the incision to the scalp (Fig. 1). If the internal jugular vein is being used, the needle also pierces the belly of the sternocleidomastoid muscle. After the obturator is removed, the silicone rubber catheter (for an infant, the internal diameter is 0.025 in. and the outside diameter is 0.047 in.) is passed through the needle. When the needle is withdrawn, the catheter resides in its subcutaneous tract. Prior to cannulation, the vein is ligated distally and an incision is made between this point and a proximal controlling ligature. If the internal jugular vein has been selected, ligature of the vein can sometimes be avoided by passing the cannula into the vein through an incision made in the center of a pursestring suture. The jugular vein is then cannulated and the tubing advanced to the region of the right atrium (approximately 5 cm in an infant). Occasionally, some manipulation is necessary to obtain entry into the superior vena cava from the ex-

ternal jugular vein. The exact location of the catheter is confirmed radiographically by taking a single x-ray with the catheter filled with radiopaque contrast material.

The silicone rubber catheter slides easily and is soft and compressible. Therefore, the ligature which holds it in the lumen of the vein must be tied so that it neither occludes the lumen of the tube nor allows the catheter to slip out of the vessel. To fix the tube properly, we use a circular sleeve of silicone rubber to which Dacron wings have been bonded (manufactured by Medical Devices, Inc.) (see Fig. 3). After venous cannulation, the sleeve of silicone rubber is opened, and at its entrance into the jugular vein, the venous catheter is placed within the lumen of the sleeve. The venous catheter is glued to the sleeve with silicone cement. The Dacron wings are sutured with nonabsorbable sutures to the surrounding tissues. To remove the central venous line, the sleeve and its Dacron attachments must be cut by opening the neck wound under local anesthesia.

Antibiotics are administered only when indicated by the child's primary illness, but not specifically to prevent sepsis which might occur from the presence of a central venous line.

An antibacterial ointment and sterile dressing are applied to the

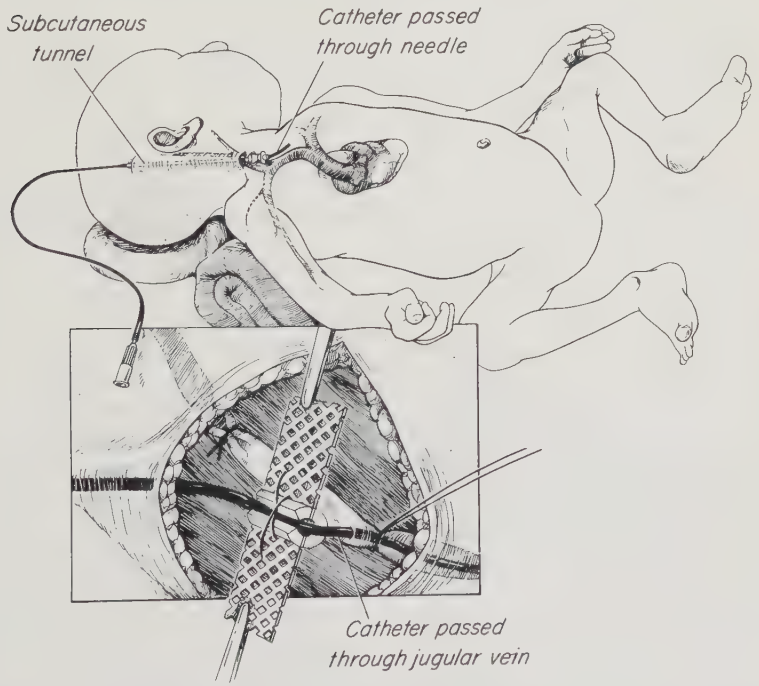

Figure 1. Insertion and fixation of silicone rubber central venous catheter in an infant. The catheter is passed through a hollow needle which has created a subcutaneous tunnel from the venous cutdown site in the neck to the appropriate skin exit site behind the ear. After the vein is intubated a vein flange of silicone rubber with Dacron wings is attached to the tubing and secured in the neck wound to prevent accidental dislodgement of the catheter. (Figs. 1 and 2 reproduced from Ghadimi, H.: Total Parenteral Nutrition – Premises and Promises. New York, John Wiley & Sons, 1975, pp. 445–482. Used with permission.)

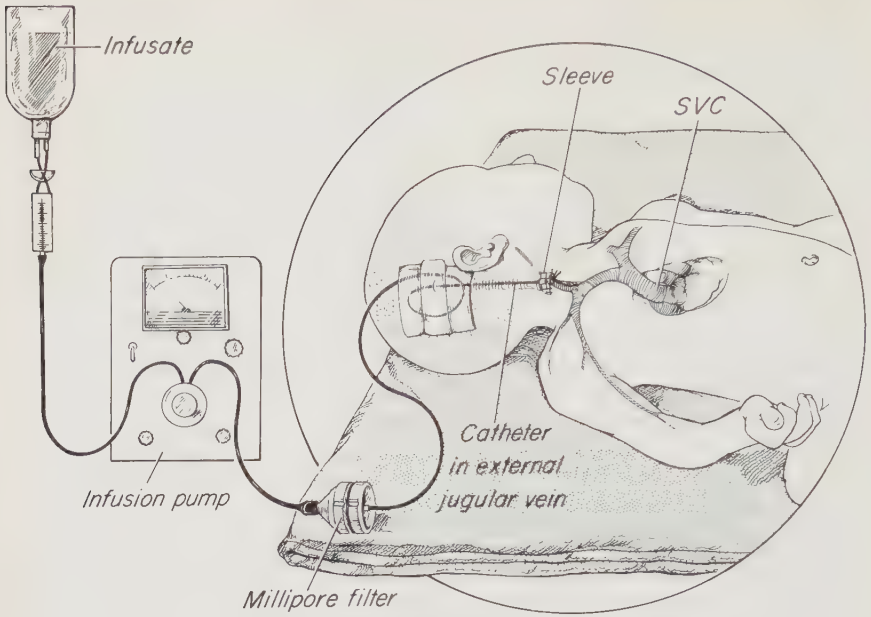

Figure 2. System for long-term central total parenteral nutrition. Amino acid-dextrose infusate flows through a calibrated buret. Infusion pump ensures uniform hourly flow rate. The Millipore filter in the circuit will remove any microorganisms which may have contaminated the system. The venous catheter enters the scalp behind the ear. It is secured in the vein by a silicone rubber sleeve (vein flange) which is buried beneath the skin incision in the neck. The appropriate position of the catheter in the superior vena cava is confirmed radiographically.

skin exit site, and to avoid accidental displacement, a coil of catheter is included in the dressing. Every 2 days, the dressing is removed aseptically, the skin cleansed with an antiseptic, and a sterile dressing and antibacterial ointment reapplied. Povidine-iodine (Betadine) ointment is now used routinely because of its effectiveness against both bacteria and fungi. Before the infusion is started, a Millipore filter (0.22μ) is placed in-line to remove particulate matter and/or microorganisms which may have contaminated the solution. A calibrated buret is placed in the circuit to monitor the volume delivered accurately. Injection tubing (T-connector, manufactured by Abbott Laboratories) may also be added to the circuit so that intravenous drugs can be given aseptically above the filter. All intravenous tubings and the bottle of infusate are changed daily. Since the high sugar content of these infusates supports the growth of yeast, the external surfaces of all intravenous tubings should be washed with Betadine solution twice a day to remove traces of nutrient solution which may have inadvertently dripped from the bottle onto the tubing. Betadine ointment should also be applied to all joints in the circuit to prevent entry of microorganisms at these points.

The infusate must be delivered at a slow uniform rate to ensure proper utilization of the glucose and amino acids. In the small infant this is most readily accomplished by the use of a constant-infusion pump. In some centers, gravity drip is used for older patients. The entire system, locally referred to as the "lifeline," is shown in Figure 2.

In many institutions, patients on TPN are treated in one intensive care area. Because of our geographic and departmental structure and the diversity of disease states, we have found it more efficient to treat these children on the medical or surgical divisions where they would be ordinarily. To provide standardized optimal care, we employ a nurse who oversees the care of every patient on TPN. This nurse makes rounds twice a day to check the intravenous tubings, pumps, and infusates. She advises and instructs the floor nurse and house staff on proper techniques and management and is on call for any unforeseen mechanical problems which may develop. On alternate days, she changes the dressings over the central venous catheter and is the only person who is permitted to draw blood from the central venous line to obtain samples for routine weekly analysis or for additional studies which may be required by special protocol.

Peripheral Feeding with Fat

The technique of infusion is depicted in Figure 3. In infants, a 21 to 23 gauge scalp vein needle (sometimes even a 25 gauge needle) is inserted into a peripheral vein, usually in the scalp, and the intravenous tubing from the bottle containing the amino acids is connected to this needle. The tubing from the Intralipid bottle is then inserted into the rubber nipple at the end of the tubing from the first bottle ("piggybacked") and is secured to this tubing with tape. A calibrated buret is

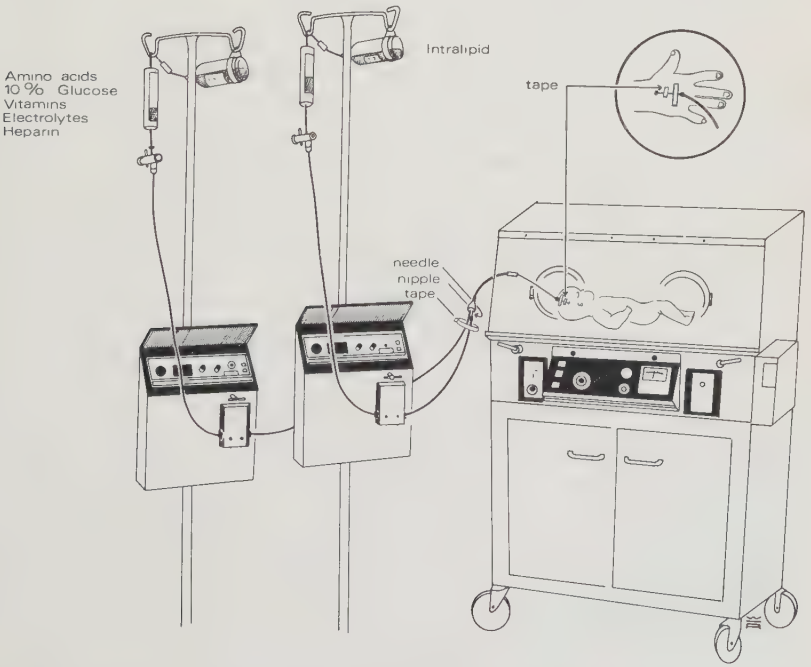

Figure 3. Technique of intravenous feeding with Intralipid. In infants, a needle is inserted into the scalp; in older children, the veins on the dorsum of the hand are generally used. See text for details.

placed in each intravenous line and both bottles are infused over a 24-hour period using two separate constant infusion pumps. The 24-hour infusion with two separate pumps is employed to insure proper utilization of the administered fat, glucose, and amino acids. No filters are used since these would block the infusion of the fat. The needle usually requires changing every 3 to 4 days because of infiltration. In children, the same technique is used except that the dorsum of the hand rather than the scalp is used.

Peripheral Feeding without Fat

The techniques involved here are no different from those used for routine intravenous infusions. The entire solution is contained in one bottle and is infused into a small needle placed into a peripheral vein in the scalp or extremity. A Millipore filter (0.22μ) is placed in-line and the infusion is run over 24 hours for the various reasons already discussed. The intravenous sites last 24 to 48 hours and are changed promptly when signs of infiltration or phlebitis are noted. Warm soaks placed over the infiltrated skin reduce the swelling rather quickly. Rarely, a small skin slough results which heals fairly rapidly with local care.

METABOLIC OBSERVATIONS

Clinical measurements which are essential include daily body weight, accurate volume of urine, and other body fluid losses. The urine sugar content is monitored at each voiding. The important blood tests and the frequency of study in the usual patient are given in Table 5. More frequent monitoring of some variables may be necessary in patients with specific metabolic abnormalities such as those with renal or hepatic disease.

Weight changes during the period of intravenous feeding will vary with the patient's overall clinical status. Weight gains comparable to

Table 5. *Blood Values Monitored Routinely During Total Parenteral Nutrition*

FREQUENCY OF MONITORING		
At start of therapy and weekly	At start of therapy and every 2 weeks	As indicated
Na, K, Cl	SGOT, LDH, alkaline phosphatase	Copper
Urea	Bilirubin	Zinc
Glucose	Creatinine	Iron
Magnesium		Ammonia
Calcium, phosphorous		Osmolarity
Total protein		pH
Hgb., Hct., Wbc.		
Blood culture		
Candida precipitins		

those of normal infants may be expected in those children who are not malnourished at the time intravenous feedings are instituted or in whom sepsis is not a part of the clinical picture (Fig. 4). In the patient with infection or another clinical problem which increases metabolic requirements, a flatter growth curve may be observed. A significant weight gain in the first 2 weeks of therapy is not usually seen in those infants and children who are severely depleted at the start of treatment. The weight gains observed with the three different techniques are comparable, averaging 20 to 30 gm per day in the neonate.

Despite the variations in weight curves, positive nitrogen balance has been noted in all patients studied in detail. Fecal loss of nitrogen is usually negligible since stools are infrequent and scanty during periods of intravenous feeding. Urinary amino acid losses have been found to be negligible and not sufficient to produce osmotic diuresis except in infants weighing under 1 kg and in those children with severe renal disease.

In most patients, the large quantity of intravenous glucose is well tolerated without the addition of exogenous insulin. Blood sugar levels remain in the normal range, but urinary sugar content usually varies between 0 and 3+ by the Clinitest method. Urinary sugar levels are generally highest during the first day or two of treatment. Qualitative urine sugars consistently above 3+ may cause an osmotic diuresis and often signal the likelihood of bloodstream infection, especially in the patient

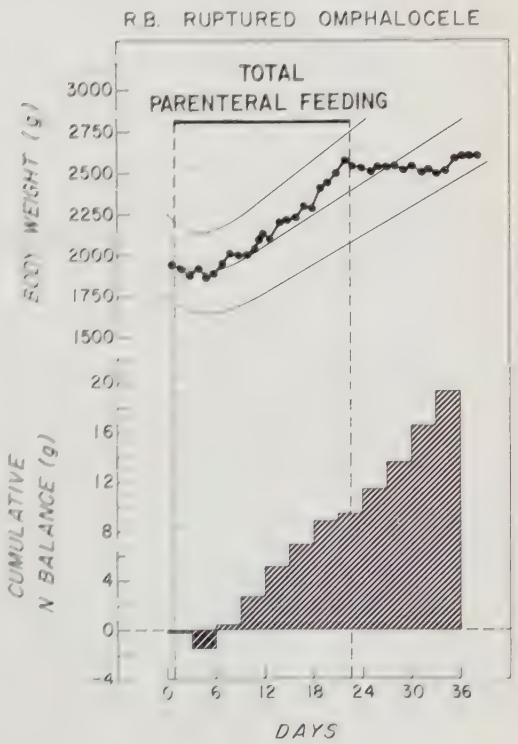

Figure 4. Weight response of a 1.9 kg neonate to total parenteral feeding during multistaged repair of an omphalocele, with daily weights charted adjacent to expected weight curves for normal infants (cumulative nitrogen balance is indicated). A central venous catheter was inserted, and first-stage repair with gastrostomy was performed on the first day of life. Total parenteral feedings were continued for 19 days during three subsequent operative procedures. Daily weight increases paralleled those of a normal infant. When oral feedings were started, weight gain diminished, although positive nitrogen balance persisted. (Reproduced from Filler, R. M., Eraklis, A. J., Rubin, V. G., and Das, J. B.: Long-term parenteral nutrition in infants. N. Eng. J. Med., 281:589–594, 1969. Used with permission.)

who has been treated for many days without glycosuria. A temporary decrease in hourly infusion rate or use of a more dilute solution usually corrects the problem if it is not due to sepsis.

Water balance is maintained even in infants weighing under 2.5 kg and in those following surgery despite the infusion of this hypertonic solution. Urinary solute excretion of this intravenous diet is usually greater than that observed during oral feeding, but this increased load does not exceed the concentrating capability of the normal infant kidney.

COMPLICATIONS

Metabolic Complications

The metabolic complications that have occurred during TPN in infants and children are listed in Table 6. The potential complications are many, but most patients tolerate these intravenous mixtures quite well. Although some of the complications are unavoidable, most can be prevented by appropriate adjustments of the infusate based on careful clinical monitoring.

Glucose intolerance and hyperglycemia have been observed (in the absence of sepsis) only in low-birth-weight premature infants and others with severe renal and central nervous system abnormalities. In some of these cases, widely fluctuating blood sugar levels even with the use of insulin forced us to abandon the intravenous feeding program.

Although hypoglycemia has been reported when TPN is stopped abruptly, we have not observed this complication despite the many accidental interruptions of the infusion. Nevertheless, when TPN is no longer needed and oral intake starts, we recommend a gradual weaning from the intravenous diet to avoid this potential complication.

Metabolic acidosis has occurred as a complication of TPN. Although the amino acids in all presently available TPN solutions challenge the patient with a large acid load, on our current formulas most patients do not become acidotic. The acidity and free water content of our mix-

Table 6. *Metabolic Complications*

Persistent hyperglycemia and glycosuria
Osmotic diuresis
Postinfusion hypoglycemia
Acidosis
Hyperammonemia
Amino acid toxicity
Hypomagnesemia
Hypocupremia
Essential fatty acid deficiency
Hypocalcemia, hypercalcemia, hypophosphatemia
Hepatic impairment (toxic)
Hypercholesterolemia
Hypertriglyceridemia

tures is such that the acid-base regulatory mechanisms of the average infant and child are adequate to compensate for the acid load. When a more concentrated preparation (5.25 per cent Fre-Amine and 25 per cent glucose) was used in the past, smaller infants developed acidosis with serum pH as low as 7.0. In susceptible individuals such as the low-birth-weight premature infant and those with renal or hepatic disease, frequent monitoring of blood pH is necessary to avoid acidosis even when using our present mixtures.

Hyperammonemia has been reported in infants generally less than 6 months of age.[13, 14] It has been postulated that it is due to one or a combination of the following factors: (a) infusion of large quantities of ammonia which are present in protein hydrolysate solutions; (b) the administration of a diet which contains inappropriate proportions of amino acids; (c) subclinical liver disease or hepatic immaturity; and (d) arginine deficiency. We have measured blood ammonia at varying intervals after the institution of TPN in 23 infants. In 12 infants with elevated SGOT, LDH, and bilirubin, blood ammonia levels were normal. In 11 others with normal liver function tests, blood ammonia was elevated (75 mg per cent) in two, but normal in the others. Clinical signs of ammonia intoxication were never evident in any of these 23 patients or in any other patient whom we treated.

Plasma and urine amino acids were measured in a small group of children, and in some, abnormal serum values were detected. Histologic examination of the central nervous system in children who died while on TPN did not reveal the hypothalamic lesions produced in mice by the administration of protein hydrolysate or acidic amino acids.[16]

Hypomagnesemia causing seizures was seen in several patients early in our experience. In each case, the patient had prolonged diarrhea prior to the institution of TPN. Typically, seizures occurred within the first week of TPN therapy. Seizures due to hypomagnesemia have been largely eliminated since the magnesium content of the standard infusate has been increased and additional magnesium has been administered at the start of therapy to patients with hypomagnesemia due to chronic diarrhea.

Copper deficiency has been observed recently as a result of chronic diarrhea and diets with insufficient copper such as TPN programs.[1, 15] Copper is now given routinely to all patients. The features which have been ascribed to lack of copper include anemia, neutropenia, hypoproteinemia, osteoporosis, deep pigmentation of skin and hair, hypotonia, and psychomotor retardation. In the malnourished patient with depleted copper stores, overt signs of copper deficiency are most likely to develop when weight gain and growth occur on a high-caloric, high-protein diet low in copper. In the last 3 years, serum copper was measured in 76 infants and children on TPN. In 23 cases, serum copper was low and ranged from 20 to 75 μg per cent (normal 87 to 150 μg per cent). Nineteen of these 23 patients were on TPN because of chronic diarrhea and had a low serum copper at the onset of therapy. The other four were not depleted at the start, but developed low serum copper before copper was added to the intravenous mixture routinely from 1 to 5 months after the

start of therapy. Anemia, which was noted in 15 of these copper-deficient patients, was due at least in part to copper deficiency. Clinical evaluation for bone abnormalities was not performed. Increase in the serum copper was noted in depleted patients who were treated with small quantities of copper sulfate by mouth and in the others when oral feedings resumed.

Serum zinc was measured in conjunction with serum copper in these 76 patients. Low serum zinc was never observed (even after 6 months of TPN), even when the only source of zinc available was from transfusion. Nevertheless, zinc is now given to all patients in the trace metal solution.

Clinical signs of essential fatty acid deficiency were apparent in only two children on the central feeding program, although in our series and others,[17] serious abnormalities in serum lipids have been noted after prolonged fat-free therapy. Each patient had been on TPN longer than 3 months when a severe generalized skin rash typical of essential fatty acid deficiency developed. Fortunately, at this stage of therapy, each infant was able to tolerate a small quantity of fat by mouth and the skin lesions soon disappeared. Essential fatty acid deficiency did not develop in any of the patients on Intralipid nor was this syndrome seen in the infants receiving sunflower seed oil cutaneously. Most of the patients on Intralipid had normal triglyceride and cholesterol levels in their serum; however, a few, who were on hyperalimentation for greater than 1 month, ran serum triglycerides in the range of 300 to 350 per cent (normal 150 to 250 mg per cent) and serum cholesterols of 150 to 250 mg per cent (normal 100 to 150 mg per cent). These mild elevations returned to normal once the Intralipid was stopped.

Hypocalcemia, hypercalcemia, and hypophosphatemia and hyperphosphatemia have all occurred in patients being fed solely by vein.[19, 20] Quantities of calcium and phosphorus in our present intravenous mixtures appear sufficient to avoid these problems in the vast majority of patients treated. Weekly monitoring of serum calcium and phosphorus suffices to detect an abnormality which might require modification in the quantities of calcium and phosphorus infused.

Signs of abnormal liver function have often been observed during TPN. Transient hepatic enlargement, with or without abnormal liver function tests, was noted during the first week of therapy in most small infants. Variable and intermittent elevations of serum SGOT, LDH, and bilirubin occurred throughout the course of treatment in many patients. The histologic appearance of the liver either by biopsy or autopsy fails to reveal a consistent pathologic alteration. Although the nature of the underlying clinical problems for which TPN is required offers sufficient explanation for the liver abnormalities noted in some of the patients, in others such a cause is not apparent. We must remain alert to the possibility that these liver abnormalities may be due to a harmful substance in the infusate or to a dietary imbalance. The liver abnormalities seen with and without Intralipid appear to be the same and disappear once the intravenous feeding is stopped. In addition, intravenous fat pigment is usually seen in the Kupffer cells of the liver in most pa-

tients on Intralipid for longer than 1 month. This pigment deposition appears to have no effect on liver functions.

About 80 per cent of the patients on Intralipid develop a peripheral eosinophilia in the range of 5 to 10 per cent and in a few this may rise to 35 per cent. There are no clinical manifestations of this abnormality such as skin rashes, urticaria, etc.

Osmotic diuresis secondary to significant glycosuria occasionally occurs when the 20 per cent glucose infusate is used. The premature infant with under-developed renal tubules is most susceptible to this complication. This phenomenon is not seen with peripheral hyperalimentation because of the lower tonicity of the infusate.

No instance of fluid overload in the form of pulmonary edema, peripheral edema, or congestive heart failure was seen in any of the patients treated with the three various techniques. This is especially important to note in the group managed with peripheral hyperalimentation without fats, in which the volume of fluid infused is quite high.

Technical Complications

Many of the early technical problems associated with the catheter have now been either corrected or reduced in frequency. The use of polyvinyl catheters was associated with a high incidence of sterile inflammation and thrombosis; nonreactive silicone rubber catheters have minimized these hazards. Transitory arrhythmias may occur during the insertion of the catheter, especially if the tip enters the heart. The position of the catheter tip must be checked radiographically to be certain that the irritating hyperosmolar solution is delivered into the superior vena cava and not into a smaller vein with a lower blood flow, such as the hepatic. Dislocation of the catheter is less frequent since a vein flange is used to secure it.

Venous Perforation. A complication which is reported in the literature, has not occurred in our patients. Thrombosis of the vein in which the catheter resides can occur, especially in the critically ill patient with sepsis and inadequate circulation. When thrombosis occurs in the superior vena cava, it is better tolerated than in most other vessels. Although evidence of thromboembolism has been noted at autopsy in children dying with the central venous catheter in place, manifestations of this phenomenon in vivo are rare. Among the important factors in the prevention of venous complications are the use of jugular veins rather than femoral or umbilical veins for intubation, x-ray control of the catheter position, the avoidance of sepsis, and the use of a silicone rubber catheter.

No case of phlebitis was seen in the patients treated with Intralipid peripherally despite the fact that the entire infusate is slightly hypertonic. Intralipid in some unknown fashion appears to protect the vein from phlebitis. When infiltration does occur, it is usually bland and the fluid is rapidly reabsorbed. Phlebitis is seen occasionally in the patients fed peripherally without fat but disappears when the infusion site is changed. In the 35 patients treated with peripheral hyperalimentation without fat, three cases of skin slough at the infusion site were seen; two healed spontaneously and one needed skin grafting.

Infection

Sepsis remains the major complication of central TPN in the pediatric patient. Long-term indwelling venous cannulas are a well-documented source of bloodstream infection. Organisms may enter the bloodstream along the catheter tract or with a contaminated intravenous solution. The catheter, a foreign body in the bloodstream, may act as a focus for bacterial growth even if organisms enter from a distant septic site. To minimize the risk of sepsis, the following measures and precautions should be taken. Catheters should be placed under aseptic conditions in an operating room. Silicone rubber catheters rather than polyethylene or polyvinyl catheters should be used because they cause less tissue reaction and are less likely to produce a thrombus which will support the growth of microorganisms along the wall of the intubated vein. The skin exit site for the catheter should be placed in an area which can be cleansed aseptically and meticulously. Proper care of this site and all the connectors and tubings between the intravenous bottle and the patient is essential. Use of the central venous catheter for necessary blood sampling should be obtained only by properly trained personnel.

Any relaxation in strict adherence to the standard technique of catheter care is followed by a sharp rise in the incidence of infective complications. Some institutions[6] have reported such an extremely high incidence of fungal septicemia and death that treatment with TPN in such a hospital is unwarranted.

A review of the Children's Hospital Medical Center experience indicated that 42 of 264 patients (16 per cent) had one or more septic complications. The incidence of sepsis was not related to the patient's age or diagnosis. Analysis of our septic complications reveals that the likelihood of sepsis was clearly related to the duration of therapy. For each week of therapy after the first week, the risk of sepsis increases by about 5 per cent.

Fever, leukocytosis, and/or unexplained glycosuria were usually the first clues to bloodstream infection. Infection was confirmed when microorganisms were cultured from blood obtained through the central venous line. Candida was isolated in 18 blood cultures, a variety of gram-negative bacteria in nine cultures, and staphylococcus, streptococci, or diphtheroids in 20. In five cases, more than one organism was found.

Infants with proven Candida bloodstream infection were treated by removal of the central venous line; chemotherapy was usually withheld because of the toxicity of amphotericin. In those with bacterial sepsis, the line was usually withdrawn and appropriate antibiotics were given. In five patients with bacterial infection, the venous catheter was left in place and antibiotic therapy alone was curative. Recovery from septicemia was usually evident within 24 hours. Forty of 42 patients survived the septicemia episode although six eventually died of their primary disease. Two deaths could be attributed directly to catheter sepsis. One infant, a newborn with gastroschisis and intestinal obstruction, developed Candida septicemia on the 16th day of TPN and the line was removed. The central venous line was inserted 5 days later, but sep-

ticemia recurred and the infant expired. The other death occurred in an 8-week-old infant with a complicated esophageal abnormality including tracheoesophageal fistula and massive chalasia. The patient developed Candida septicemia on the 22nd day of TPN. The line was removed, blood cultures became negative, and a second line was inserted 10 days later. On the following day, bilateral overwhelming monilial pneumonia due to embolization of a septic thrombus in the superior vena cava resulted in the death of this infant. Therefore, despite the relatively high incidence of infection, the overwhelming majority of affected patients recover without serious sequelae.

Invasive sepsis related to hyperalimentation was not seen in any of the 80 patients treated with Intralipid nor in any of the infants and children managed with peripheral intravenous feeding without fat.

When patients are properly selected for treatment and appropriate precautions are exercised, the benefits far outweigh the risks. It has been most gratifying to see that parenteral nutrition has been responsible for the salvage of many children who would have died of starvation in the past.

REFERENCES

1. Ashkenazi, A., Levin, S., Djaldetti, M., Fishel, E., and Benvenisti, B.: The syndrome of neonatal copper deficiency. Pediatrics, 52:525, 1973.
2. Borresen, H. C., Coran, A. G., and Knutrud, O.: Metabolic results of parenteral feeding in neonatal surgery: A balanced parenteral feeding program based on a synthetic L-amino acid solution and a commercial fat emulsion. Ann. Surg., *172*:291, 1970.
3. Coran, A. G.: The intravenous use of fat for the total parenteral nutrition of the infant. Lipids, 7:455, 1972.
4. Coran, A. G.: The long-term total intravenous feeding of infants using peripheral veins. J. Ped. Surg., *8*:801, 1973.
5. Coran, A. G.: Total intravenous feeding of infants and children without the use of a central venous catheter. Ann. Surg., *179*:445, 1974.
6. Curry, C. R., and Quie, P. G.: Fungal septicemia in patients receiving parenteral hyperalimentation. N. Engl. J. Med., *285*:1221, 1971.
7. Dudrick, S. J., Steiger, E., and Long, J. M.: Renal failure in surgical patients: Treatment with intravenous essential amino acids and hypertonic glucose. Surgery, *68*:180, 1970.
8. Dudrick, S. J., Wilmore, D. W., Vars, H. M., and Rhoads, J. E.: Long-term total parenteral nutrition with growth, development, and positive nitrogen balance. Surgery, *64*:134, 1968.
9. Dudrick, S. J., Wilmore, D. W., Vars, H. M., and Rhoads, J. E.: Can intravenous feeding as the sole means of nutrition support growth in the child and restore weight loss in an adult? An affirmative answer. Ann. Surg., *169*:974, 1969.
10. Filler, R. M.: A new method of fixation of silicone rubber catheters for long-term hyperalimentation. J. Ped. Surg., *8*:395, 1973.
11. Filler, R. M., Eraklis, A. J., Rubin, V. G., and Das, J. B.: Long-term parenteral nutrition in infants. N. Engl. J. Med., *281*:589, 1969.
12. Fox, H. A., and Krasna, I. H.: Total intravenous nutrition by peripheral vein in neonatal surgical patients. Pediatrics, 52:14, 1973.
13. Ghadimi, H., Abaci, F., Kumar, S., and Rathi, M.: Biochemical aspects of intravenous alimentation. Pediatrics, *48*:955, 1971.
14. Johnson, J. C., Albritton, W. L., and Sunshine, P.: Hyperammonemia accompanying parenteral nutrition in newborn infants. Pediatrics, *81*:154, 1972.
15. Karpel, J. T., and Peden, V. H.: Copper deficiency in long-term parenteral nutrition. Pediatrics, *80*:32, 1972.
16. Olney, J. W., Ho, O. L., and Rhee, B.: Brain-damaging potential of protein hydrolysates. N. Engl. J. Med., *289*:391, 1973.
17. Paulsrud, J. R., Pensler, L., Whitten, C. F., Stewart, S., and Holman, R. T.: Essential fatty

acid deficiency in infants induced by fat-free intravenous feeding. Am. J. Clin. Nutr., 25:897, 1972.
18. Press, M., Hartop, P. J., and Prottey, C.: Correction of essential fatty-acid deficiency in man by the cutaneous application of sunflower-seed oil. Lancet, *1*:579, 1974.
19. Shils, M. E.: Guidelines for total parenteral nutrition. J.A.M.A., 220:1721, 1972.
20. Travis, S. F., Sugarman, H. J., Ruberg, R. L., Dudrick, S. J., Papadopolous, M. D., Miller, L. D., and Oski, F. A.: Alterations of red-cell glycolytic intermediates and oxygen transport as a consequence of hypophosphatemia in patients receiving intravenous hyperalimentation. N. Engl. J. Med., 285:763, 1971.

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Gastrointestinal Bleeding in Children

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The spectrum of diseases which result in gastrointestinal hemorrhage in children is quite unlike that seen in adults.[9] Carcinoma is rare, while medical diseases and coagulation disorders are sufficiently common that the surgeon must be wary of operating on a child for bleeding without an excellent indication.[6]

Mothers tend to exaggerate the volume of blood their child has lost. One must make every effort to pin down the exact amount of bleeding by specifically inquiring whether it is a few drops on the surface of the stool, a tablespoon full, or a cup. An estimate of the volume of blood lost in the stool or through vomiting, together with observation of the child's vital signs, indicates the magnitude of the hemorrhage. A child is capable of intense vasoconstriction to maintain his blood pressure. Pallor, tachycardia, poor capillary and venous filling, and a depressed urinary output are better signs of shock than the blood pressure. Carefully consider the child's body weight and estimate his total predicted blood volume when evaluating the severity of his hemorrhage. A newborn infant's blood volume is equivalent to 8½ per cent of his body weight in kilograms. This decreases to 7½ per cent by 4 or 5 years of age. Thus, a 100 ml blood transfusion in a 10 kg child is the equivalent of a 700 ml transfusion in an adult.

Direct inspection of the blood will give a clue as to its source. Hematemesis always indicates a bleeding point proximal to the ligament of Treitz. Bright red blood which streaks the surface of the stool originates from the anorectal area. On the other hand, massive upper gastrointestinal hemorrhage may stimulate hyperperistalsis so that unaltered blood appears in the stool. Brick red blood is characteristic of a Meckel's diverticulum, and bloody mucus or a currant jelly stool is classic for an intussusception. Acute bloody diarrhea suggests an infectious disease such as shigellosis while chronic diarrhea with bleeding should make one think of ulcerative colitis in any age group. In general, the darker the blood in the stool, the higher it originates from the gastrointestinal tract. A nasogastric tube should be passed during any significant episode of

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Figure 1. Melanin spots in the mouth of a child with the Peutz-Jehgers syndrome.

gastrointestinal hemorrhage. The aspiration of gross blood or "coffee ground" material immediately localizes the bleeding point to the esophagus, stomach, or duodenum. If the nasogastric tube drains clear, bile-stained material, the source of hemorrhage is distal to the ligament of Treitz.

The physical examination may provide us with a number of clues. Search the skin and mucous membranes for hemangiomas or melanin spots of the Peutz-Jehgers syndrome (Fig. 1). A palpable spleen in the presence of upper gastrointestinal hemorrhage is practically diagnostic for esophageal varices. Bruises, petechiae, or hemorrhage from the nose or mouth are clues to systemic bleeding disorders. Visual inspection of the anus may reveal an anal fissure, cryptitis, or even a severe diaper rash which oozes blood. *Never* omit a rectal examination—60 to 75 per cent of rectal polyps are within reach of the examining finger.

BLEEDING IN THE NEWBORN INFANT

During birth a baby may swallow sufficient maternal blood to cause black stools or even hematemesis. The Apt test distinguishes adult from fetal hemoglobin.[2] It is performed by mixing one part of bloody stool or vomitus with five parts of water. This mixture is centrifuged for 1 or 2 minutes at 2000 rpm. The supernatant is mixed with 1 ml of 0.1 normal sodium hydroxide. Fetal hemoglobin remains pink, while adult hemoglobin changes to a dirty brown color.

Hemorrhagic disease of the newborn is now exceedingly rare since neonates are given vitamin K in the delivery room. However, one mg of vitamin K should be given empirically and the same dose is continued for 5 days. Sherman and Clatworthy reviewed 94 infants under 4 weeks of age with gastrointestinal bleeding.[26] None had a surgically correctible

lesion. Anorectal trauma, hemorrhagic disease, and swallowed maternal blood were the most common identifiable causes for the bleeding. The maternal ingestion of salicylate causes loss of platelet aggregation in babies and severe gastrointestinal hemorrhage has been reported in an infant born to a mother who had ingested salicylate prior to delivery.[12] Most often no specific source for the bleeding is ever found. It stops spontaneously and never recurs.

Treatment of the newborn infant during the phase of active bleeding consists of transfusing fresh whole blood or fresh frozen plasma and packed red cells to maintain his vital signs and a urinary output of 1 ml per kg per hour. The blood is carefully warmed prior to administration, especially if large amounts are given rapidly. Give 10 mg of calcium gluconate with every 100 ml of blood. Poor tissue perfusion and rapid blood transfusion may result in metabolic acidosis. This is corrected with a slow infusion of sodium bicarbonate, while monitoring the capillary pH. A nasogastric tube is inserted even if there is no hematemesis. It is irrigated with 1 per cent sodium bicarbonate and the stomach lavaged until clear if any blood is aspirated. Continued intermittent aspiration provides an index to the rapidity of bleeding. When the infant is stable a barium meal is performed.

Anorectal Fissures

When a mother says that her baby has rectal bleeding and is constipated, the diagnosis is almost certain to be an anal fissure. Most often the fissure starts with the passage of a hard stool which tears the sensitive squamous lining of the anal canal. There is anal spasm, and the baby cries with pain at each bowel movement. He quickly learns to hold back his stool with the result that he becomes more constipated; a vicious cycle of hard stools, bleeding, and pain takes place.

The diagnosis is made by spreading the baby's buttocks until the anal canal is visible. Most babies strain down enough so that the fissure is clearly visible. Treatment consists of keeping the stool soft with mineral oil and the application of zinc oxide ointment. Some anal fissures become chronic and recalcitrant to these simple remedies. It then becomes necessary to dilate the rectum under general anesthesia and excise the chronically scarred tissue down to the superficial anal sphincter. The resulting incision is then kept open with rectal examinations until healing is complete.

Rectal Bleeding in Older Children

Between the ages of 2 and 12 years, the most common lesion causing rectal bleeding is the juvenile polyp. A number of polyps are missed because of an inadequate proctoscopic examination on an awake, moving child, especially if poorly prepared. Consequently, perform all diagnostic proctoscopies on children under general anesthesia in the operating room where facilities are available for suction, biopsy, and fulguration. Juvenile polyps of the colon are inflammatory lesions which never become malignant and which are often self-limiting because they outgrow their blood supply and are passed spontaneously with the

stool.[13] They cause intermittent, recurrent, bright-red-to-dark bleeding with stools.

Juvenile polyps within reach of the proctoscope are removed with a snare and cautery. The pedicle may bleed vigorously but will stop with further fulguration and pressure. If one or more juvenile polyps are removed, and histologic diagnosis verified, nothing further needs to be done even if a barium enema demonstrates another polyp higher in the colon. However, if proctoscopy is negative and a barium enema reveals a polyp beyond reach of the proctoscope, it must be removed to establish a diagnosis. This is preferably done with a flexible colonoscope, but if a skilled endoscopist is unavailable, then at laparotomy through a colotomy.

Rarely, the entire colon may be studded with pedunculated juvenile polyps.[25] These result in chronic anemia as well as hypoalbuminemia from protein losing enteropathy. In this situation, a subtotal colectomy is indicated.

The polyps of Peutz-Jehgers syndrome are really hamartomas. They may be scattered throughout the gastrointestinal tract, but most are in the small intestine where they continually bleed causing chronic anemia. Intussusception may occur and result in several intestinal resections for gangrenous bowel. A gastrointestinal series with a careful small bowel follow-through will demonstrate the polyps. Proctoscopy and gastroscopy may be performed to learn the true extent of the polyposis. These polyps should be removed at an elective operation. Bowel is intussuscepted through several enterotomies; large pedunculated polyps are removed by ligation of the base and excision.[23] Smaller polyps are simply fulgurated. With time and patience, the entire small intestine may be explored and all the offending polyps removed (Fig. 2). A child with multiple or familial polyposis of the colon may present with rectal bleeding. He is more likely to complain only of loose, frequent stools or be asymptomatic. This disease is clearly distinguished from juvenile polyposis because the colon is studded with innumerable polyps—these are adenomatous and premalignant lesions. A subtotal colectomy with a low ileoproctostomy may be performed. The rectal stump must then be examined at frequent intervals to fulgurate recurrent polyps and to detect a carcinoma. Ravitch and, more recently, Soper have recommended colectomy, with an endorectal pull-through of the ileum to completely eliminate the polyp-bearing colonic mucosa.[24, 27]

UPPER GASTROINTESTINAL BLEEDING

Bleeding peptic ulcers of the stomach and duodenum in children are usually associated with steroid therapy or stress such as burns, head injuries, and meningitis.[21] The incidence of upper gastrointestinal hemorrhage in burned children has been reduced by avoiding aspirin as an antipyretic agent and the routine introduction of a milk drip via a nasogastric tube as soon as the initial paralytic ileus has passed. When hematemesis or melena does occur in a child with a pre-existing stressful illness, a nasogastric tube is inserted and the stomach irrigated with

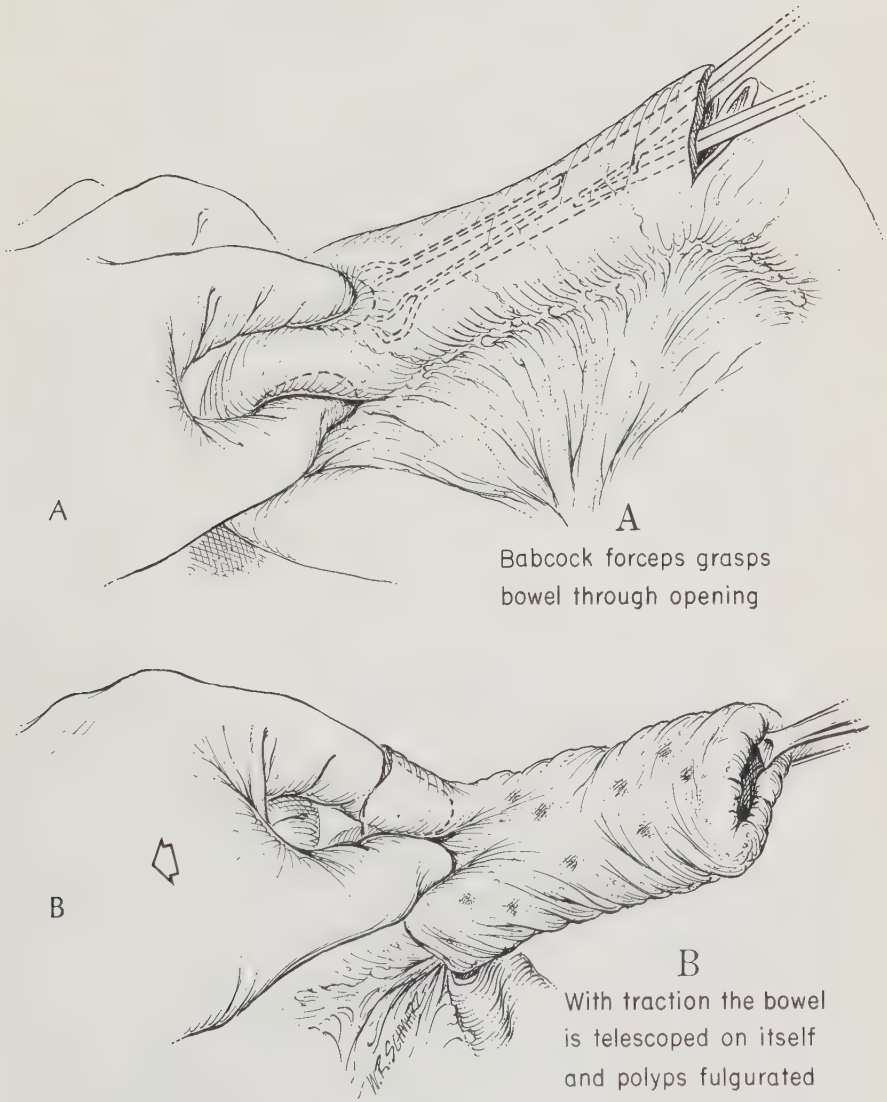

Figure 2. Illustration of the technique to intussuscept the small intestine through enterotomies to examine the mucosa for polyps or hemangiomas.

iced 1 per cent sodium bicarbonate. When the child's estimated blood volume has been replaced by transfusion and hemorrhage continues, an operation is indicated. These sick children are frequently in negative nitrogen balance and at risk to eviscerate postoperatively; for this reason, we have adopted a right, extended subcostal incision to explore the stomach and duodenum. The bleeding point is found through a gastroduodenotomy and is suture ligated. A vagotomy and pyloroplasty will reduce the risk of further bleeding.

Esophageal Varices

Most children with portal hypertension have an extrahepatic portal vein obstruction. The most commonly accepted explanation for this lesion is thrombosis of the vein with secondary cavernomatous transformation.[8] A history of exchange transfusions at birth through the umbilical vein or umbilical sepsis would support this concept. Only a few children, however, have this history and others have had anomalies elsewhere in their vascular system suggesting a congenital basis for the obstruction.[22] Prolongation of life in children with previously early fatal conditions has produced a number of children with intrahepatic portal obstruction and esophageal varices. Included are those who are living longer after operations for biliary atresia; children with cystic fibrosis of the pancreas develop biliary cirrhosis because of obstruction due to viscid secretions and a few children in long term remission from leukemia are developing hepatic fibrosis due to methotrexate toxicity. Esophageal varices are likely when the child presents with hematemesis and an enlarged spleen. An esophagogram nearly always demonstrates varices and the diagnosis may be confirmed by esophagoscopy if there is doubt.

Treatment during an acute bleeding episode consists of mild sedation, blood replacement, and gastric lavage with cold 1 per cent sodium bicarbonate. Continued bleeding can be controlled with a child-sized Sengstaken-Blakemore tube. Shunt operations are rarely successful in young children because the portal vein is unavailable and other venous anastomoses less than 1 cm in diameter are rarely successful. Medical management is therefore important to carry these children along until they are 8 to 10 years of age. These patients must avoid aspirin and all aspirin-containing medications. Antacids and a bland diet are prescribed. Upper respiratory infections which seem to trigger bleeding episodes are vigorously treated with bed rest, humidity, and antibiotics and cough suppressants.

A splenoportogram is essential to map the portal system and to determine the size of the portal and splenic vein prior to any operation. The splenoportogram in Figure 3 demonstrates a typical portal vein obstruction.

Children with extrahepatic portal vein obstruction require some form of splenorenal or a mesocaval shunt. The most important natural collaterals are through the spleen, the splenic vessels and the left renal vein. The spleen and these collaterals should be preserved because a satisfactory shunt will also relieve the hypersplenism which regularly accompanies portal hypertension.[28] Currently, a side-to-side splenorenal shunt or a mesocaval shunt is providing the most satisfactory results in

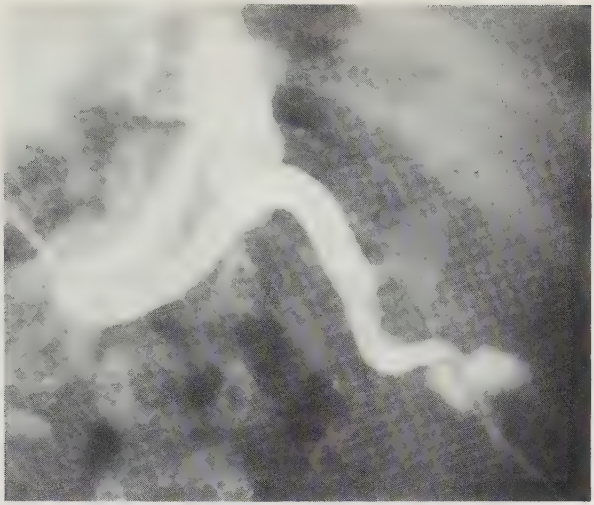

Figure 3. Splenoportogram demonstrating extrahepatic obstruction of the portal vein.

our hands. When the spleen has been sacrificed and shunt operations have failed to relieve repeated hemorrhages, resection of the distal esophagus and proximal stomach with the interposition of colon is indicated.[16] Fortunately, Myers and Johnson observed that as these children grow older, many spontaneously improve as they develop natural collaterals.[20]

Meckel's Diverticulum

Ectopic gastric acid-secreting mucosa at the tip of a Meckel's diverticulum may result in a bleeding ulcer either in the adjacent ileum or in the diverticulum itself. The pattern of bleeding is similar to that of any other peptic ulcer. It is episodic rather than chronic and may be massive. Classically, the mother finds a large, brick red, bloody stool in the diaper. The infant becomes pale, has tachycardia, and his bleeding usually stops spontaneously allowing time to obtain coagulation studies, proctoscopy, and gastrointestinal roentgenograms to rule out other lesions. X-rays are valueless in making the diagnosis; however, 99_m technetium scanning may demonstrate a Meckel's diverticulum because this radioactive substance is excreted by gastric mucosa.[30] Unfortunately, there are reports of both false positive and false negative scans.[7] Clinical judgment based on the episodic pattern, rate, and volume of blood loss is more reliable than any other diagnostic test now available. It is probably best to wait for a second episode of hemorrhage before recommending an operation in order to be certain that there is a significant lesion. The diverticulum is found on the antimesenteric border of the ileum within 2 feet of the caecum. It may be densely adherent to the mesentery and may be easily missed unless every inch of bowel is meticulously examined. If the bleeding ulcer is in the ileum adjacent to the diverticulum, it must be included in the resection. The bowel is then closed transversely with one layer of nonabsorbable sutures. If the child

is in good condition his appendix should be removed. If no diverticulum is found, the small intestine is examined for polyps, hemangiomas, or duplications. Previous roentgen studies should have ruled out lesions in the stomach and colon.

MISCELLANEOUS

Intestinal Hemangiomas

Intestinal hemangiomas are an important source of both recurrent and chronic bleeding. Abrahamson and Shandling reviewed 65 cases of intestinal hemangiomatosis and described a triad of symptoms.[1] Forty-nine per cent of their patients had cutaneous lesions, all had gastrointestinal bleeding, and phleboliths were frequently visible on plain roentgenograms of the abdomen (Fig. 4). The possibility of an intestinal hemangioma in the absence of skin lesions or phleboliths is an indication for celiac and mesenteric arteriograms, since many hemangiomas are small submucosal lesions which will not be visible on barium studies. Even with an extensive preoperative work-up, the surgeon must

Figure 4. Plain film of the abdomen demonstrating calcification with multiple intestinal and retroperitoneal hemangiomas in a 14-year-old boy.

be prepared to inspect the mucosal surface of the stomach as well as that of the entire small intestine and colon. The hemangiomas may be removed and the mucosa closed or small lesions are simply suture ligated. Mellish removed 200 hemangiomas from the gastrointestinal tract in one child and another required five operations before she was completely free from serious hemorrhages.[19] The management of children with multiple hemangiomas is complicated by the frequent occurrence of thrombocytopenia because of excessive consumption of blood coagulation components.[15, 29] This is further reason for the routine search for coagulation disorders in children with unexplained gastrointestinal bleeding. Esophagitis secondary to a sliding hiatus hernia must always be considered in anemic children with occult blood in their stool. These patients vomit and in early life a hiatus hernia can simulate pyloric stenosis. Later, they develop esophagitis, are anemic, and have frequent respiratory infections because of regurgitation and aspiration. They rarely vomit gross blood, but on careful questioning the history of "coffee ground" emesis is frequently obtained. When a hiatus hernia is suspected, the radiologist must be warned to pay particular attention to the esophagogastric junction and to perform cine studies. Frequently, all that is seen will be gastroesophageal reflux and the stomach is observed about the diaphragm in only a few frames. Esophagoscopy should be performed to evaluate the degree of esophagitis or stricture. In infancy, a hiatus hernia is treated by keeping the baby continuously in an upright position. Continued vomiting, anemia, and persistent esophagitis are indications for hiatal hernia repair.[5] Currently, in our hands, the Nisson fundoplication together with closure of the hiatus is curative.

Abdominal Trauma

Hematobilia in children usually follows blunt trauma to the abdomen. We have also cared for a boy who had hematobilia secondary to multiple liver abscesses. Either the liver may have been fractured or there may have been an intrahepatic hematoma which erodes its way into a bile duct. The child complains of cramping right upper quadrant pain and then vomits blood. There is tenderness in the right upper quadrant because of the liver injury and a tensely distended gallbladder. A liver scan will reveal the intrahepatic defect, but a selective hepatic angiogram is essential to localize the source of hemorrhage (Fig. 5).

At operation, the gallbladder and common bile duct are found to contain blood. We have been successful with suture ligation of the false aneurysm in two patients, although it may be necessary to perform a hepatic lobectomy to control the bleeding.

Systemic Diseases

In addition to the specific lesions which may bleed in childhood, there are a large number of systemic diseases which may be accompanied by gastrointestinal bleeding. Surgeons must be aware of these hematologic, infectious, and immunologic conditions in childhood in order to avoid a needless, and possibly harmful, operation.

Anaphylactoid purpura or the *Henoch-Schoenlein syndrome* may present with gastrointestinal bleeding and abdominal pain, mimicking

Figure 5. Selective hepatic arteriogram with a false aneurysm from the right hepatic artery. This was treated by opening into the hematoma and suture-ligating the bleeding point.

an intussusception prior to the onset of other clinical symptoms. The diagnosis rests on the appearance of the distinctive purpuric skin lesions which are raised purplish spots appearing on the legs and the buttocks. There is also painful swelling of the joints, hematuria and hypertension secondary to renal involvement, and sometimes testicular tenderness and swelling. The bleeding and abdominal pain are secondary to a generalized vasculitis of small vessels in the intestinal submucosa. There are no distinctive abnormalities in the hematologic profile. Corticosteroid therapy will alleviate both the bleeding and abdominal pain, but the child must be closely observed because a submucosal hematoma may become the lead point of an intussusception.[4] The hemolytic-uremic syndrome is characterized by a microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure.[18] It most commonly occurs in infants and young children and is preceded by gastroenteritis or a mild upper respiratory infection. Rarely, bloody diarrhea may be so severe as to stimulate fulminant ulcerative colitis.[3] Hypertension is common and central nervous system manifestations of somnolence, coma, and convulsions further complicate the clinical picture. Failure to appreciate the significance of early oliguria often results in

fluid overload and congestive heart failure. Disseminated intravascular coagulation is probably the basic process which leads to thrombocytopenia and hemorrhage. Azotemia and red blood cell fragmentation always occur. Peritoneal dialysis has decreased the mortality rate in this disease.

Milk allergy, intolerance to the proteins of cow's milk, can cause occult or gross rectal bleeding. Often this is with mucus on the stools and diarrhea. The onset of symptoms is usually within the first 6 weeks of life. These infants may have recurrent respiratory infections, otitis media, wheezing, and atopic dermatitis. Sigmoidoscopy reveals edematous colon mucosa with petechial hemorrhages. High milk antibody titers may be formed, but a firm diagnosis rests on the clinical demonstration of subsidence of symptoms after milk elimination and recurrence within 48 hours after its reintroduction. A wide range of milk substitutes is available for infants. The intolerance usually disappears by 1 or 2 years of age.

The *Aldrich-Wiskott syndrome,* a sex-linked recessive condition in infants, is characterized by draining ears, an excematoid dermatitis, and bloody diarrhea. Proctoscopically, the colon mucosa is friable and may resemble ulcerative colitis. These infants have thrombocytopenia and pursue a relentless downhill course and die with overwhelming infections.[17]

Other genetic disorders which may be accompanied by gastrointestinal bleeding are the *Ehlers-Danlos syndrome* and *pseudoxanthoma elasticum.* The associated skin and joint pathology should suggest these diagnoses.

Parasitic and infectious diseases in children who have recently immigrated from tropical countries must be considered. Hollander et al. diagnosed and successfully treated a 32-day-old Puerto Rican infant who had massive intestinal hemorrhage secondary to infestation with the hookworm. Necator americanus,[14] shigellosis, and endamoebae histolytica can also cause either bloody diarrhea or blood-streaked stools. It behooves the physician to obtain stool specimens for culture, ova, and parasites when studying a child with unexplained rectal bleeding.

Endoscopy

The flexible fiberoptic endoscopes which have been useful in locating the source of gastrointestinal bleeding in adults are now being miniaturized and adapted to pediatric use. Colonoscopy has allowed the removal of polyps above the reach of the standard proctoscope and gastroduodenoscopy has proved superior to roentgenograms in the diagnosis of gastric and duodenal ulcers in children.[10]

CONCLUSION

A carefully performed history and physical examination, together with a few well-planned laboratory tests and roentgenograms, will solve most gastrointestinal bleeding problems in infancy and childhood, obviating the need for "the exploratory operation" which is often fruitless and may be harmful.

REFERENCES

1. Abrahamson, J., and Shandling, B.: Intestinal hemangiomata in childhood, a syndrome for diagnosis: A collective review. J. Ped. Surg., *8*:4, Aug. 1973.
2. Apt, L., and Downey, W. S. Melena neonatorum: The swallowed blood syndrome. J. Ped. Surg., *47*:6, 1955.
3. Berman, W., Jr.: The hemolytic uremic syndrome: Initial clinical presentation mimicking ulcerative colitis. J. Ped., *81*:275–278, 1972.
4. Borges, W. H.: Anaphylactoid purpura. MED. CLIN. N. AM., *56*:201–206, 1972.
5. Cahill, J. L., Aberdeen, E., and Waterston, D.: Results of surgical treatment of esophageal hiatus hernia in infancy and childhood. Surgery, *66*:597–602, 1969.
6. Cain, A. S., and Longino, L. A.: Carcinoma of the colon in children. J. Ped. Surg., *5*:5, Oct. 1971.
7. Chaundhuri, T. K., and Christie, J. H.: False positive Meckel's diverticulum scan. Surgery, *71*:323, 1972.
8. Clatworthy, H. W., Jr., and Boles, E. T., Jr.: Extrahepatic portal red block in children: Pathogenesis and treatment. Ann. Surg., *150*:371, 1959.
9. Collins, R. E.: Some problems of gastrointestinal bleeding in children. Arch. Dis. Child., *46*:10, 1971.
10. Gans, S. L., Ament, M., Christie, D. C., and Liebman, W. M.: Pediatric endoscopy with flexible fiberscopes. J. Ped. Surg., *10*:375–380, June 1975.
11. Gryboski, J. D.: Gastrointestinal milk allergy in infants. Pediatrics, *40*:354–362, 1967.
12. Haslam, R. R., Ekert, H., and Gillam, G.: Hemorrhage in a neonate due to maternal ingestion of salicylate. J. Ped., *84*:556–557, 1974.
13. Holgerson, L. O., Miller, R. E., and Zintel, H. A.: Juvenile polyps of the colon. Surgery, *69*:288–293, Feb. 1971.
14. Hollander, M., Tobingo, R., and Stankewick, W. R.: Successful treatment of massive intestinal hemorrhage due to hookworm infection in a neonate. Trop. Pediat., *82*:2, 332–334, 1975.
15. Kasabach, H. H., and Merritt, K. K.: Capillary hemangioma with extensive purpura. Am. J. Dis. Child., *59*:1063, 1940.
16. Koop, C. E., and Kaviamian, A.: Reappraisal of colonic replacement of distal esophagus and proximal stomach in the management of bleeding varices in children. Surgery, *57*: 454–456, 1965.
17. Krivit, W., and Good, R. A.: Aldrich's syndrome (thrombocytopenia, eczema and infection in infants). J. Dis. Child., *97*:137–153, Feb. 1959.
18. Lieberman, E.: Hemolytic uremic syndrome. J. Ped. Surg., *80*:1–16, 1972.
19. Mellish, R. W.: Multiple hemangiomas of the gastrointestinal tract in children. Am. J. Surg., *121*:412–417, April 1971.
20. Meyers, N. A., and Johnson, M. J.: Extrahepatic portal hypertension in children. J. Ped. Surg., *8*:4, Aug. 1973.
21. Raffensperger, J. G., Condon, J. B., and Greengard, J.: Complications of gastric and duodenal ulcers in infancy and childhood. Surg. Obstet. Gynec., *123*:1269–1274, Dec. 1966.
22. Raffensperger, J. G., Shkolnik, A., Boggs, J., and Swenson, O.: Portal hypertension in children. Arch. Surg., *105*:249–254, Aug. 1972.
23. Raffensperger, J. G., Moncado, R., and Seeler, R. A.: The Acute Abdomen in Infancy and Childhood. Philadelphia, J. B. Lippincott & Co., 99, 1970.
24. Ravitch, M. M., and Sabiston, D. C.: Anal ileostomy with preservation of the sphincter. Surg. Gynec. Obstet., *84*:1095, 1947.
25. Sachetello, C. R., and Hohn, S. C.: Juvenile gastrointestinal polyposis in a female infant: Report of a case and review of the literature of a recently recognized syndrome. Surgery, *75*:101–114, Jan. 1974.
26. Sherman, N. J., and Clatworthy, H. W., Jr.: Gastrointestinal bleeding in neonates: A study of ninety-four cases. Surgery, *62*:614–619, Oct. 1967.
27. Shirazi, S. S., Soper, R. T.: Endorectal pull-through procedure in the surgical treatment of familial polyposis. J. Ped. Surg., *8*:5, Oct. 1973.
28. Tank, E. S., Wallin, W., Jr., Turcotte, J., et al.: Surgical management of bleeding gastroesophageal varices in children. Arch. Surg., *98*:451–456, 1969.
29. Wacksman, S., Flessa, H. C., Glueck, H., and Will, J. J.: Coagulation defects and giant cavernous hemangiomas. Am. J. Dis. Child., *111*:71, 1966.
30. Wine, C. R., Nahrwold, D. L., and Waldhouse, J. A.: Role of technetium scan in the diagnosis of Meckel's diverticulum. J. Ped. Surg., *9*:6, Dec. 1974.

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Urinary Diversion and Undiversion in Children

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The urinary tract accounts for a large share of surgically correctable pathology in childhood. Techniques for managing urologic disorders have changed greatly in the past 10 to 20 years. For example, in the mid-1950's severe obstructive uropathy and neurogenic bladder were often best treated by prolonged catheter drainage and suppressive antimicrobial therapy, although it was well recognized that prolonged intubation of the urinary tract was inevitably accompanied by infection. Thus, when the ileal loop or conduit was devised by Bricker,[4] it soon found widespread application in childhood both in patients with neurogenic bladder and cases of severe obstructive uropathy with damaged upper tracts. In the late 1950's the great importance of vesicoureteral reflux came to the forefront when routine cystography became a part of urinary tract evaluation in children. Soon ureteral reimplantation became a part of the surgeon's armamentarium,[11, 13, 19, 26, 34, 42] and then repair of megaureters of various types.[3, 14, 21, 28, 35, 39, 41, 50] Tubeless, temporary, or permanent diversion then became widely used in the 1960's.[27, 29, 30, 40] Recently, in the 1970's the practice of reconstructive pediatric urology has changed much of the above.[1, 15-17] Indications for urinary diversion have changed as well as methods used when it is needed. Further, a second look at previously diverted children has unearthed many who can be reconstructed in light of currently available techniques.[7, 18, 20] This article will present some of our own current thoughts on diversion and undiversion.

URINARY DIVERSION

Indications

Severe obstructive uropathy was formerly a prime indication for urinary diversion "to save the remaining upper tract function," but this is no longer tenable in most cases. Ureters which are refluxing can be reimplanted. Ureters which are dilated and tortuous can be shortened, tapered,

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and reimplanted. The new fiberoptic pediatric endoscopes make possible precise endoscopic destruction of urethral valves, the treatment for which was previously not so successful. Very importantly, long-term follow-up of diverted children, particularly those with ileal loops, has shown a high rate of persisting bacilluria, and gradual upper tract deterioration[6, 8, 37, 43, 44] which was hopefully to be prevented by diversion in the first place. In children with ileal loops, deterioration in many undoubtedly results from low-grade bacilluria together with reflux. Indeed, free loop-to-ureter reflux on loopogram has always been considered desirable to exclude lower ureteral obstruction. Reflux of bowel mucus to the renal pelvis provides a nidus for stone formation so often seen in patients with loops.

Myelodysplasia causing neurogenic bladder has been a major indication for permanent diversion of the urinary tract both to provide a means for getting the youngsters dry and to preserve the upper tracts. I believe that this will remain a reasonable approach for the time being in many cases, yet newer developments have made diversion more selective. Scott et al.[47] introduced an artificial sphincter which has shown promise in some of these children. Intermittent catheterization can maintain sterile urine and acceptable continence in some of these patients. Pharmacologic stimulation of the bladder can be helpful in some cases. Electrical stimulation may prove of value in the future. Endoscopic incision of the bladder neck may improve emptying of neurogenic bladders in some children.

Bladder exstrophy has been a cause for urinary diversion despite great interest in primary functional closure of the exstrophied bladder.[5, 9, 32, 52] Regarding primary closure, it is clear that the chance for complete success in this undertaking is small, even in the hands of enthusiasts who gained great experience operating on large numbers of these children. Megalli and Lattimer,[36] for example, reported one success in 89 cases; they concluded that ileal loop diversion is preferred. Even those who continue to espouse primary closure exclude many exstrophied bladders because they are too rudimentary to consider reconstruction. Primary ureterosigmoidostomy has many advocates;[2, 48] experience has shown many excellent results, but unfortunately also many dismal failures with renal deterioration.

We are currently treating patients with exstrophy of the bladder by an alternative method, staged ureterosigmoidostomy.[25] In new cases a nonrefluxing colon conduit is performed at about 1 year of age. This provides a means for getting the child dry by wearing an appliance. About 3 to 6 months later the exstrophied bladder is closed and the genitals are repaired. The child has a reasonable appearance by the time he is a toddler. There is then a relatively normal early development—going to school, etc.—albeit with a bag on the abdomen. In contrast, children treated by primary closure or other methods in my experience often spend many of their early developmental years in hospitals, with recurrent urinary infections, etc. When the child is 4 to 6 years of age and has rectal continence, the conduit is detached from the abdominal wall and joined end-to-side to the rectosigmoid colon. Urine is then passed per rectum. This approach has two distinct advantages over primary ureterosigmoidostomy in early infancy. First, it gives long-term follow-up of the ureterosigmoid-

ostomies, in a defunctioned loop of bowel, to make certain there is no obstruction or reflux which can quickly destroy the kidneys. Only after several years of radiographic follow-up are the ureterosigmoidostomies subjected to the contaminated fecal stream. Secondly, it defers channelling the urine to the rectum until such an age as the child has achieved continence. Combined leakage of feces and urine in the early developmental years is a malodorous social disaster which can lead to ostracism by one's peers.

Many youngsters with exstrophy of the bladder have been treated by ileal loop urinary diversion, either as a primary procedure or attempted primary closure with failure. In the past 5 years we have operated on 15 of these children, removing their ileal loops and constructing a nonrefluxing colon conduit. After 6 to 12 months, to make certain that there is no low pressure ureteral reflux, or obstruction, a second stage is performed, joining the conduit to the colon.[25]

Pelvic malignancy, particularly sarcoma botryoides of the genitourinary tract, can require anterior exenteration which is another indication for urinary diversion in childhood. Some of these patients have been managed by primary ureterosigmoidostomy, but this carries two disadvantages. First, there are the potential complications of joining the ureter to a contaminated colon. Second, if there is recurrence of tumor, ureterosigmoidostomy may be contraindicated. Our own approach has been to use a nonrefluxing colon conduit for diversion, subsequently following the child for a prolonged period to make certain that there is no recurrence or radiation proctitis, and then later joining the conduit to the rectosigmoid.

Techniques for Urinary Diversion

ILEAL LOOP. The ileal loop has been used extensively in the past, but, in our opinion, it is currently an outmoded procedure for use in young patients with a long life expectancy. Laboratory study by Richie et al.[45, 46] showed significant protection to the kidneys by diverting the urine using a nonrefluxing colon conduit as compared to the ileal conduit which has reflux. If an ileal conduit must be used (patients with an abnormal colon), we construct nipple ureter-to-loop anastomoses to prevent reflux.

COLON CONDUIT. Use of colon for a urinary conduit is not a new procedure. It was used by Gross[12] in the 1940's, but never gained much popularity. Mogg[38] reported its use in children with myelodysplasia. Since 1971[22] we have preferred it for several conditions which include: (1) new patients with bladder exstrophy, (2) exstrophy treated by previous ileal loop, (3) malignancy requiring anterior exenteration, (4) ileal loop with upper tract deterioration, and (5) patients with neurogenic bladder requiring permanent urinary diversion.

OPERATIVE TECHNIQUE FOR COLON CONDUIT

Technical aspects of the operation and its variations are shown in Figures 1 to 5. Preoperatively the bowel is thoroughly prepared by cleansing enemas, liquid diet for 3 or 4 days, and neomycin by mouth, as well as by rectal irrigation 1 day

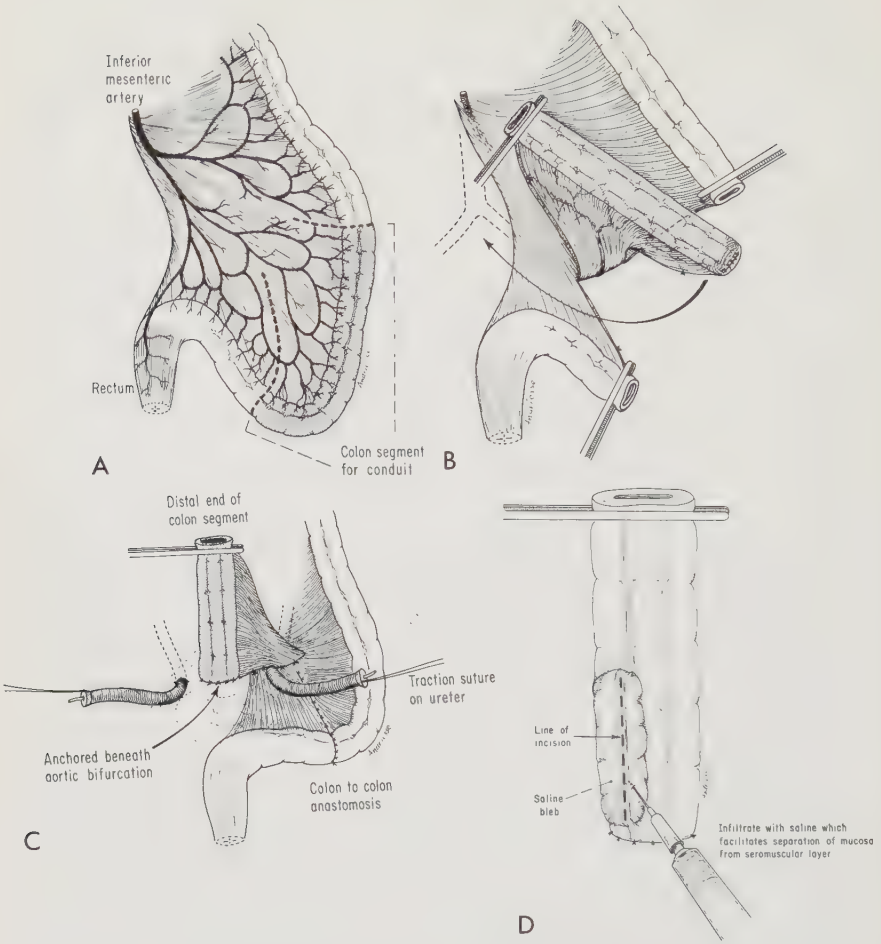

Figure 1. *A*, A segment of sigmoid colon is selected, with appropriate blood supply. The mesentery of the conduit should be maintained as broad as possible, incising the mesentery only enough to give sufficient mobility to anchor the conduit at the desired location. The bowel segment should be of ample length to allow for some shortening from contraction of the taenia, especially when it is contemplated that the conduit will later be taken down from the abdominal wall, resecting the stoma, and rejoining it end-to-side into the colon.

B, The proximal end of the conduit is closed with two layers of chromic catgut. The conduit is rotated 180° clockwise and is anchored at the aortic bifurcation above the sacral promontory. If one or both ureters are short, the point at which the base of the loop is anchored may vary, to be at a higher level or in a retroperitoneal gutter, and the conduit mesentery may lie better if it is *not* rotated.

C, Colon continuity is reestablished, usually taking down the splenic flexure to accomplish anastomosis without tension. Mesenteric traps are closed. The ureters lie adjacent to the base of the conduit. In mobilizing the ureters, the periureteral adventitia is preserved to insure a good blood supply.

D, Saline is injected with a 25-gauge needle to facilitate raising the lateral seromuscular flap without entry into the underlying mucosa.

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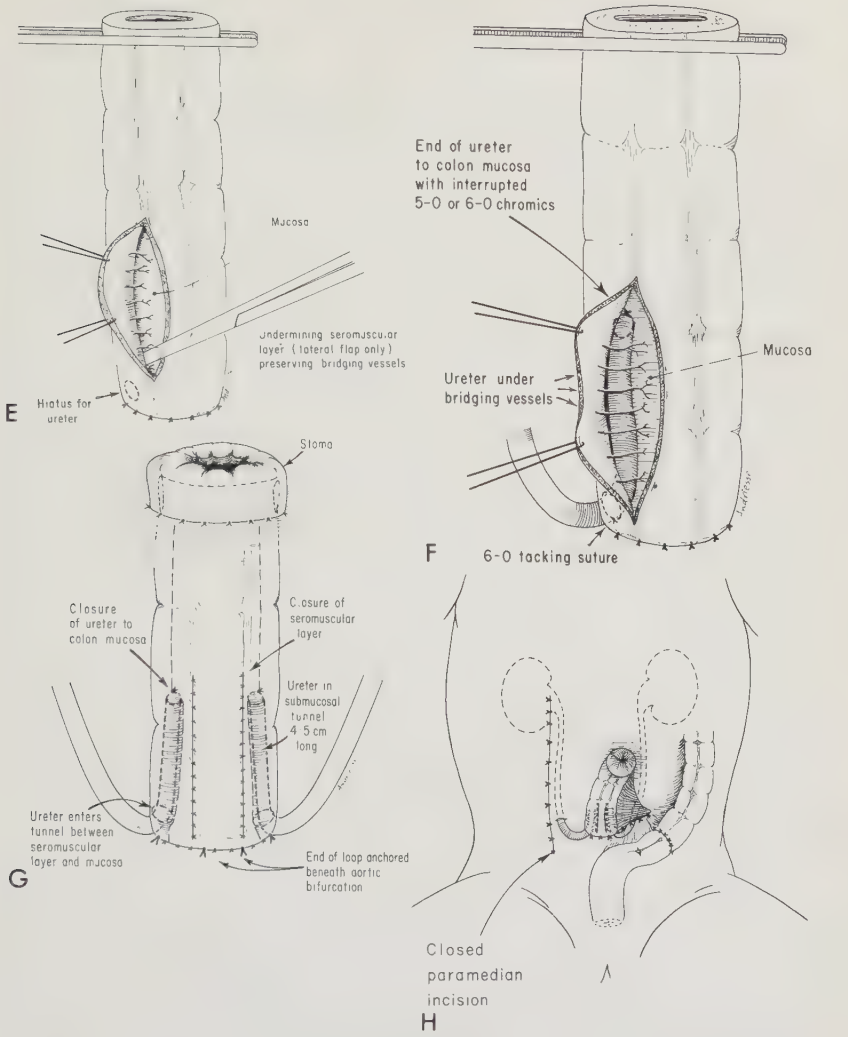
Mucosa
Undermining seromuscular layer (lateral flap only) preserving bridging vessels
Hiatus for ureter
E
Stoma
Closure of ureter to colon mucosa
Closure of seromuscular layer
Ureter in submucosal tunnel 4-5 cm long
Ureter enters tunnel between seromuscular layer and mucosa
End of loop anchored beneath aortic bifurcation
G
End of ureter to colon mucosa with interrupted 5-0 or 6-0 chromics
Mucosa
Ureter under bridging vessels
F
6-0 tacking suture
Closed paramedian incision
H

Figure 1 *Continued.* *E,* The lateral seromuscular flap is elevated, bringing into view the small blood vessels running from seromuscular layer to the underlying mucosa. This dissection is performed bluntly, and can be facilitated with "peanut" sponge dissection.

F, The ureter is brought through a separate opening in the seromuscular layer and placed beneath the bridging vessels, so that it lies in a well supported area of the bowel wall. It is anastomosed end-to-side with the colon mucosa. The ureter is usually not spatulated. A very accurate, water-tight anastomosis is mandatory.

G, Completed conduit with submucosal ureteral tunnels 4 to 5 cm long. If one anticipates later resecting the stoma to join the conduit to colon, nonabsorbable sutures should be used to close the seromuscular tunnels, for this facilitates their identification at subsequent laparotomy.

H, Completed conduit. No attempt is made to close the space on either side of the conduit, but mesenteric traps are closed.

preoperatively. Just before laparotomy a large rectal tube is inserted into the rectum. It is attached to a long tube through which the circulating nurse can irrigate and aspirate neomycin solution in case the colon is found not ideally prepared. When the colon is filled with neomycin solution by this arrangement, the surgeon can empty it and any residual fecal material by milking the intestine downward manually.

A segment of sigmoid is selected with appropriate blood supply (Fig. 1*A*). Generally, the splenic flexure is mobilized to permit end-to-end restoration of continuity without tension of descending colon to rectosigmoid. For this anastomosis we prefer two layers of interrupted arterial silk sutures on atraumatic needles. No problem has been encountered with these anastomoses. The proximal end of the sigmoid conduit is closed in two inverting layers, using chromic catgut, running the first layer and interrupting the second. Nonabsorbable suture material is not used for this closure, lest a suture work its way into the lumen of the conduit and provide a nidus for stone formation. The length of sigmoid should be amply long. In constructing ileal conduits for permanent urinary diversion, it has been a routine practice to make as short a loop as possible, to minimize the absorptive surface of bowel, particularly in patients with reduced renal function. The colon conduit has a tendency to contract in length as one is performing these operations, and so it is safer to select a fairly generous length initially, planning to trim off what is not needed when the stoma is fashioned. We recall one case in which the loop was cut too short in an obese patient where length was not sufficient to put the stoma at an ideal level on the abdominal wall. In those patients in whom the plan will be to eventually take down the stoma to anastomose the conduit back into the colon stream, i.e., patients with bladder exstrophy, or after cystectomy for cancer, the conduit is deliberately made a little longer than in a patient for whom the conduit is deemed a permanent diversion. This is done in order to allow resection of the stoma before joining the conduit to the colon.

The conduit is then usually rotated clockwise 180 degrees as shown in Figure 1*B*, so that the proximal, closed end comes to lie at the aortic bifurcation. If the conduit base is to be placed at a higher level, because the ureter is short, it may be better not to rotate it in this manner. It is anchored there with several sutures. In one case the sigmoid colon was not suitable and so we used a segment of transverse colon based on its blood supply of midcolic artery. In some patients who had undergone a prior ileal loop, the ureters were not long enough to reach the level of the aortic bifurcation, and so the end of the conduit was anchored at a high level, sometimes close to the lower pole of a kidney.

In Figure 1*C* is shown the usual anatomic relationship after fashioning the conduit, anchoring it in place, reestablishing continuity of the left colon, and mobilizing the ureters which pass close to the base of the conduit. In mobilizing the ureters, their full length should be preserved, ligating them flush with the bladder, and carefully preserving all of the periureteral adventitia which is so important with respect to maintaining a good blood supply to the ureter. A long tunnel is then created in which to lay the ureter to provide a nonrefluxing type of anastomosis. First, saline is infiltrated through a 25-gauge needle into the seromuscular layer of a taenia (Fig. 1*D*). This facilitates making a longitudinal incision without entering the mucosa. The lateral edge of this incision is then undermined, bluntly dissecting away the colonic mucosa from the overlying seromuscular layer. The medial flap is not undermined, for if that were done from both sides at the same level of the colon (since both ureters will enter at the same level), necrosis of the medial flap would likely occur. Separation of the mucosa from the seromuscular layer usually proceeds remarkably easily using a combination of blunt dissection and small "peanut" gauze sponges. The vessels bridging from the bowel wall to the mucosa can be preserved with care, and a tunnel can be made beneath them in which to place the ureter (Fig. 1*E*). This maneuver places the ureter near the mesentery of the colon conduit where it is possibly better supported. (Although we have placed the ureter beneath the vessels, as shown in Figure 1*F* in most cases, in some it has been laid on top of those bridging vessels, requiring a lesser degree of mobilization of the lateral flap. I do

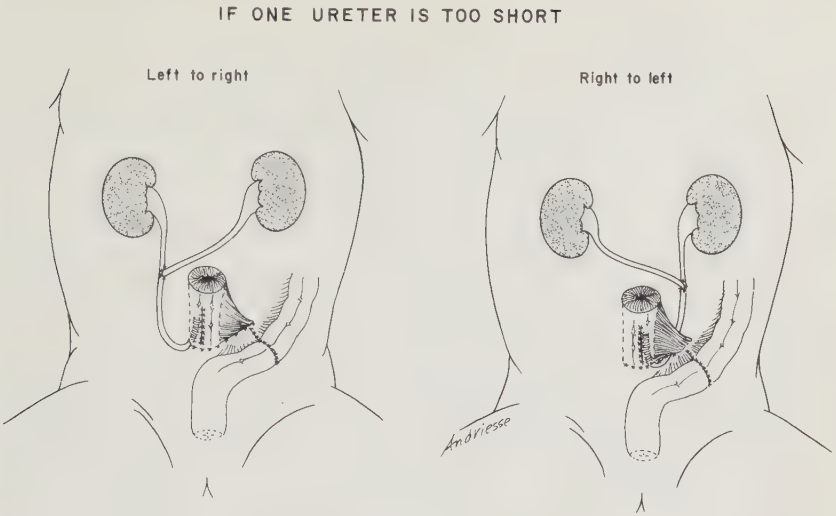

Figure 2. Transureteroureterostomy when a ureter is too short.

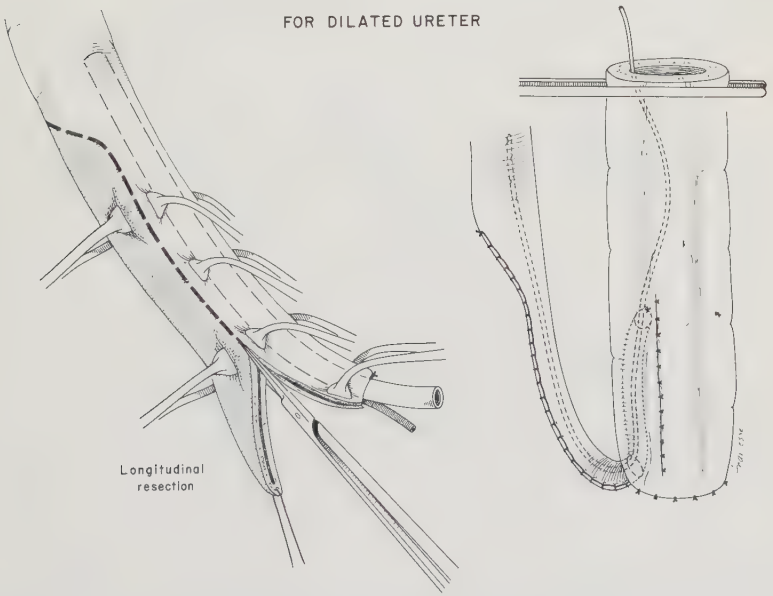

Figure 3. *A*, Tapering of the dilated ureter. Its longitudinal intramural blood supply should be preserved; this usually is located on the medial aspect of the ureter. A tapered ureter is like a pedicle flap of any tissue, i.e., its base must not be too narrow with respect to its length. If the ureter is made too narrow, its blood supply will be in jeopardy, and ischemic necrosis will result.

B, A soft, malleable plastic catheter is used to drain the ureter for 10 to 12 days. A #5 or 8 plastic feeding catheter is well suited for this.

not know whether one position is indeed better than the other but have thought that, theoretically, beneath the vessels might be better.) The ureter is anastomosed end-to-side with the mucosa at the top of the tunnel. The ureter is not spatulated. If it is a small ureter, the anastomosis is performed with 5–0 or 6–0 chromic sutures, interrupted technique. Running inverted technique can be used if the ureter is large enough to permit running closure without narrowing the caliber of the anastomosis. A drainage stent catheter is not used unless the ureter is tapered. The seromuscular layer is then closed with interrupted sutures, or a running interlocking suture, and the second ureter is joined to the conduit (Fig. 1*G*). The two ureters lie parallel about 2 cm apart, entering at the same level of the conduit. The trap beneath the mesosigmoid is closed, and a stoma is fashioned (Fig. 1*H*). In a patient previously not operated upon, this is generally in the left abdomen on the belt line. In a patient with a prior ileal conduit it may be at the site of a previous ileal stoma.

In patients with a previous ileal conduit, one or both ureters may be too short to accomplish the usual conduit construction. An alternative is anastomosis of one ureter to the conduit, with transureteroureterostomy to accomplish drainage of the other ureter, as shown in Figure 2. If the ureter to be joined to the conduit is somewhat short, the conduit can be placed moderately high in the posterior peritoneal gutter to accomplish a urterosigmoid anastomosis of adequate length without tension.

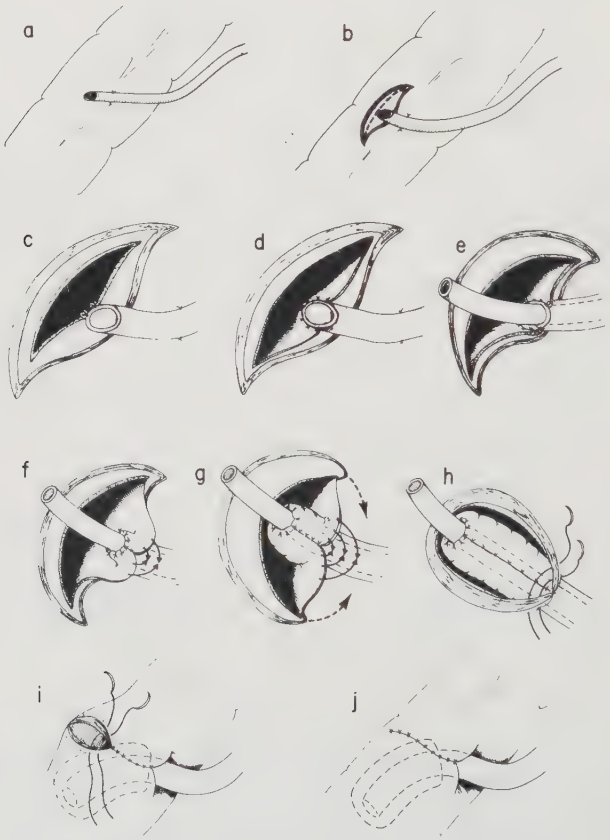

Figure 4. Mathisen method of ureterosigmoidostomy, used in five cases in which a ureter was not well suited for tunneling.

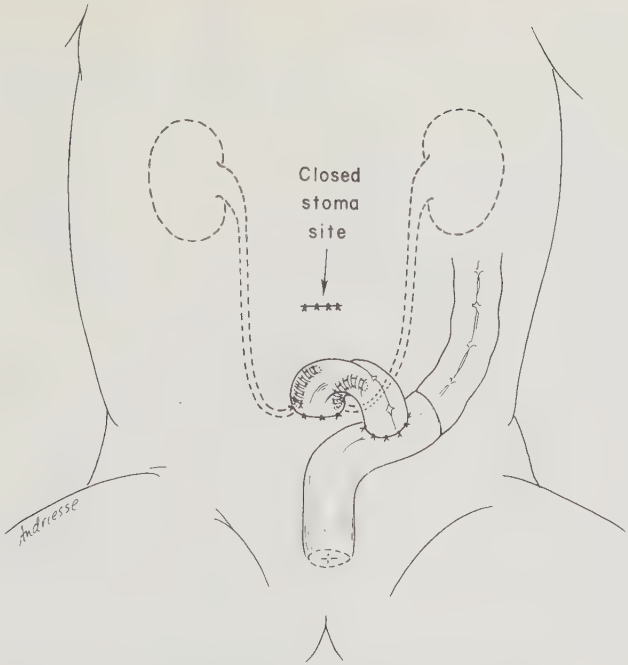

Figure 5. Subsequent implantation of conduit into the colon by end-to-side technique, using two layers of chromic catgut (running technique for the inner layer, to insure a watertight anastomosis, and interrupted sutures for the seromuscular layer).

If a ureter is dilated, it is longitudinally resected, just as in a megaureter repair as shown in Figure 3. A No. 8 plastic feeding catheter is used for temporary drainage for 10 to 12 days until this longitudinal suture line heals. It is important to preserve the vascularity of the ureter by not making it too narrow.

An alternative method of ureterosigmoidostomy is shown in Figure 4, devised by Mathisen[33] of Oslo, Norway. This has found great favor among surgeons of Europe as an excellent method of ureterosigmoid diversion. We have used it for five ureters, in circumstances when the ureter did not seem well suited for the usual long ureterosigmoid tunnel (too short, or thick walled). A nipple is fashioned which hangs in the lumen of the conduit, and prevents reflux. In our experience it is best to fashion the periureteral flap of colon a little at a time as the anastomosis progresses, in order not to make it too narrow; this flap must be amply wide to wrap around the ureter without compressing it. After the nipple is constructed, closure is carried beyond the base of the ureterocolic junction to effect closure of the colon wall. Of the five cases in which a Mathisen nipple was used, one patient has a solitary kidney, three had transureteroureterostomy of the other ureter, and one had a usual tunnel implant of the other ureter which had better length and smaller caliber.

Implantation of the conduit at a later stage into the colon is appropriate in some cases (Fig. 5). That has been accomplished in 13 of our patients. In new bladder-exstrophy patients, the conduit should not be joined to the colon until they are old enough to have a reasonable chance for learning control of liquid by rectum. In patients whose conduits include ureteral tapering, transureteroureterostomy, etc., a longer term of follow-up is desirable to make certain that all is well in terms of drainage before risking reimplantation of the conduit into the unsterile colon. Conduits should not be rejoined to the colon in patients with poor

upper tracts or faulty anorectal control. In resecting a stoma, it is important to know the location of the ureteral orifices. For this reason closure of the seromuscular tunnels is performed with fine nonabsorbable sutures which will remain visible in the future. As an additional precaution one can actually look into the conduit with a panendoscope pre- or intraoperatively to determine the location of the ureteral orifices, sometimes with the help of indigocarmine given intravenously. Also one can look down into the colon loop, after resecting the stoma, by placing small retractors inside the lumen of the conduit, to directly visualize the ureteral orifices.

Vesicostomy. Cutaneous vesicostomy has been used for both permanent and temporary urinary diversion but the stoma location leaves much to be desired, especially when the patient becomes older and develops pubic hair.

End Ureterostomy. This can provide satisfactory drainage of large ureters but should be avoided for small ureters which are prone to develop stomal stenosis. Further, the urine is often chronically infected in any diversion which drains the kidney directly to the surface without a reflux barrier in the system.

Loop Ureterostomy. Loop ureterostomy found great popularity after its introduction in 1963 by Johnston[27] who rarely uses it today (personal communication). Its use as a temporizing measure has declined greatly since surgeons have become more accustomed to direct reparative procedures. As a permanent diversion it is unsatisfactory, for the flank or loin is not ideally suited for wearing an appliance.

Nephrostomy. Nephrostomy, using a tube, is not a good method of permanent urinary diversion. It should not be overlooked, however, as a very useful maneuver when short-term diversion is required, while preparing for a reconstructive operation or immediately following a reconstructive procedure while the urinary tract is healing.

Thus, in summary, there are many methods in current use for diverting the urinary tract in children. We have not personally found it necessary to resort to temporary diversion in children with severe obstructive uropathy as advocated by some. In children requiring permanent diversion we have switched to the nonrefluxing colon conduit as the procedure of choice. The following two cases will illustrate its use:

Case 1. Neurogenic bladder treated with colon conduit urinary diversion

This youngster was referred at age 5 years (Fig. 6). A myelomeningocele had been closed at birth. She had urinary and fecal incontinence, although the latter was managed with success by a daily enema. Previous intravenous pyelogram showed severe bilateral hydronephrosis. Cystogram showed massive vesicoureteral reflux. A nonrefluxing colon conduit was performed, with tapering of the dilated right ureter. She has had an uneventful postoperative course. The I.V.P. showed great improvement. Cultures obtained from the conduit by double-catheter technique are currently negative. She is clinically well, but is maintained on low-dose prophylactic antimicrobial therapy in view of the severe upper tract damage present before referral. Her stoma has given no problems, and she is well adjusted to this form of urinary diversion.

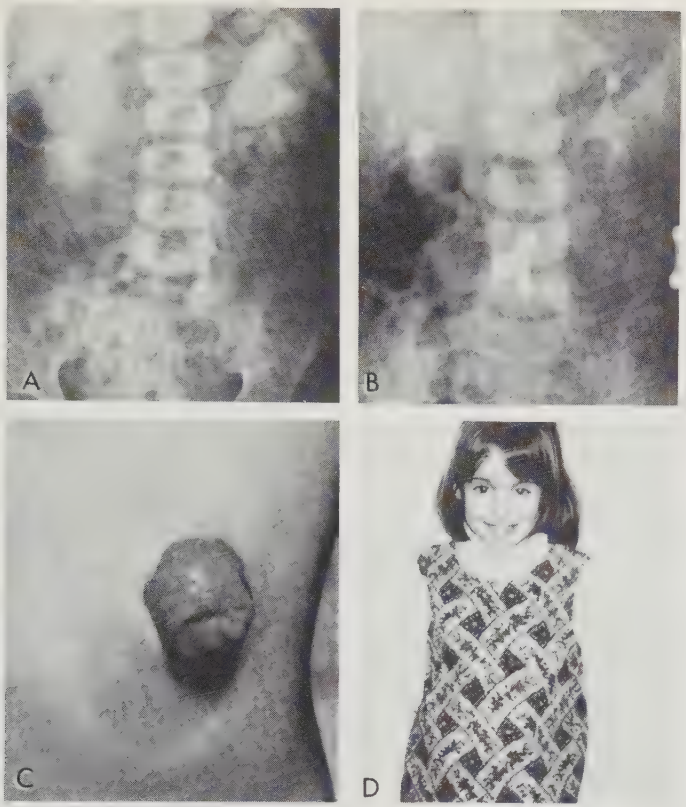

Figure 6. (Case 1) *A*, IVP preoperatively, age 4½ yr, showing severe hydronephrosis. Cystogram showed massive reflux from her neurogenic bladder. *B*, IVP 11 months after colon conduit operation, which included tapering of the right ureter. Loopogram showed no reflux, even at pressures over 60 cm of water. *C*, The colon conduit stoma. These stomas are larger and more bulky than ileal stomas, but have been uniformly more satisfactory as viewed by physicians, parents, and in particular by the children who have lived with both ileal and colon conduit stomas. There has been no problem with stomatitis, bleeding, or stenosis to date. *D*, The patient, age 6½ yr, a well child. She is maintained on low-dose nitrofurantoin.

COMMENT. It is distressing that a child with myelomeningocele should be permitted to develop this degree of severe renal damage in this day and age when so much attention has been drawn to the need to follow these children carefully from the time of birth. They require periodic cultures, intravenous pyelograms, and cystograms to make certain that they do not have infection, reflux, and upper tract changes occurring. This youngster's preoperative films serve as a poignant case in point. Although intermittent catheterization has been very helpful in managing many children with neurogenic bladder in the past few years, we felt that immediate diversion was needed in this child with already advanced upper tract changes. With recent advances in the development of implantable prostheses to control urinary incontinence, it is

possible that permanent diversion will be practiced much less frequently in the future than it is now. Although we have not had an occasion to rejoin one of these nonrefluxing conduits to the bladder, we believe that it may be possible judging from the experience with nonrefluxing ileocecal cystoplasty.

CASE 2. OLDER GIRL WITH PREVIOUS ILEAL CONDUIT FOR EXSTROPHY OF THE BLADDER

This female infant was first seen as a newborn in February 1963, with exstrophy of a tiny, rudimentary bladder. Intravenous pyelogram was normal. In October 1964, at age 20 months, ileal loop urinary diversion was performed. In June, 1965, cystectomy and epispadias repair were accomplished. I.V.P. at this time showed some dilatation of the right ureter. It was felt that this might be secondary to stenosis of the stoma, which was small, and so it was revised. Subsequent intravenous pyelograms showed even more dilatation of the right ureter, and the stoma was revised once again in June, 1967. Because the stoma tended to contract, despite two previous revisions, the family was instructed in its daily dilatation. In December 1970, the intravenous pyelogram showed still some slight dilatation of the right ureter (Fig. 7*A*). Cultures from the ileal loop showed bacteria to be present on most occasions, and so she was maintained on continuous antimicrobial therapy using nitrofurantoin. In June, 1971 the ileal loop was resected, performing a nonrefluxing colon conduit. The right ureter was short, and so the proximal end of the colon conduit was placed in the right gutter to permit ureterosigmoid anastomosis without tension. The left ureter was of ample length to bring it across the midline and construct a tunnel of satisfactory length. Intravenous pyelogram 10 days later showed moderate bilateral dilatation (Fig. 7*B*). Repeat intravenous pyelogram 6 weeks later was completely normal. Loopogram done 6 months postoperatively showed no reflux, even when the loop was distended with moderate pressure (Fig.7*C*). In August, 1972 the conduit was detached from the abdominal wall and anastomosed to the colon. She has been a completely well patient on no medication, with complete continence of urine. Intravenous pyelogram 2 years later showed normal upper tracts (Fig. 7*D*). Serum electrolyte values: sodium 144, potassium 4.1, chloride 106, CO_2 22, BUN 16 mEq per liter.

Comment. There are many children previously treated by ileal loop urinary diversion for exstrophy of the bladder, who are candidates for this type of staged diversion of the urine to the colon. A number of years ago we anastomosed an ileal loop to the colon in two patients; immediate ascending pyelonephritis occurred. The ureters can not be connected to the colon without a nonrefluxing technique if pyelonephritis is to be averted. A segment of actively peristalsing small bowel will not prevent this reflux. One might consider switching primarily from ileal conduit diversion to ureterosigmoidostomy. That has the same potential disadvantages of primary ureterosigmoidostomy, i.e., if a technical problem with anastomosis occurs, severe renal damage can ensue before it is corrected. Further, leakage of an anastomosis to the colon can give fatal peritonitis. Also, ureters which are shorter than normal would be more difficult to work with in performing primary ureterosigmoid anastomosis than previously unoperated upon ureters. We believe, therefore, that placing them first into an isolated conduit is safer, even though it requires an additional operation to subsequently anastomose the conduit to the colon.

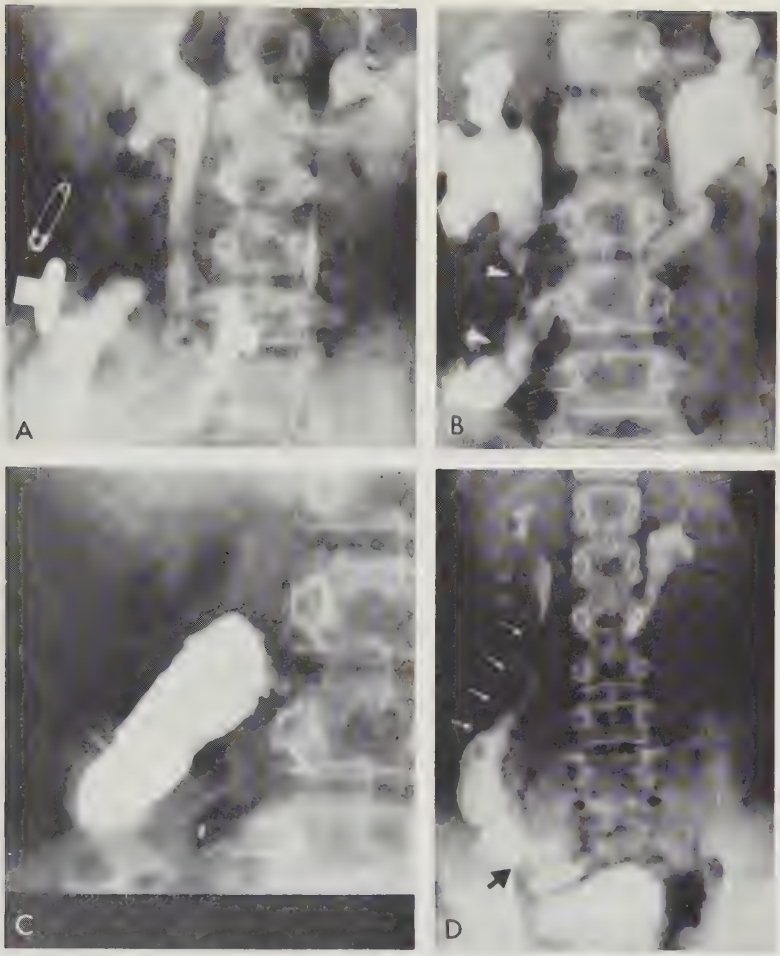

Figure 7. (Case 2) *A*, IVP of an 8-year-old child with ileal conduit. Note moderate dilatation of right ureter and renal pelvis. Two previous ileal stoma revisions. No evidence of ureteroileal obstruction, as proved by free reflux on loopogram study. Colon conduit operation performed at age 8½ yr. The right ureter was short, and so base of stoma was anchored near lower pole of right kidney, instead of at aortic bifurcation.

B, IVP 10 days after colon conduit operation, to demonstrate degree of temporary upper tract dilatation immediately after tunneling type of ureteral sigmoid anastomosis. In a defunctioned bowel loop this creates no problem. In a colon full of fecal material, this could result in immediate ascending pyelonephritis. Arrows demonstrate right ureteral tunnel.

C, Retrograde filling of loop, tamponading stoma with Foley catheter, showing no reflux, even at high pressure, greater than 60 cm of water.

D, IVP 26 months after anastomosis of conduit to rectosigmoid. Note delicate upper tracts and complete resolution of dilatation of upper tract on right, which had been persistently dilated for several years with an ileal conduit. (This dilatation disappeared shortly after colon conduit operation was performed). Small arrows point to long intramural course of right ureter in wall of conduit. Large arrow points to anastomosis of conduit to rectosigmoid. Note concentration of dye in conduit and rectum. This youngster, age 12½ yr, is completely well, on no medication, with normal continence. The quality of her life is much improved, having gotten rid of her external urinary appliance.

Angulation of the ureter is one of the complications that can occur when anastomosing ureters at different levels into the intact colon. This has been no problem when dealing with an isolated conduit. In a case not operated upon previously in which the conduit is anchored at the aortic bifurcation, the ureters are very close by, making it particularly easy to join them to the colon.

URINARY UNDIVERSION

In the past 7 years we have performed reconstructive operations on 58 children and young adults who had undergone previous urinary diversion for a variety of reasons. As shown in Table 1, the methods of diversion included: four nephrostomy, seven cystostomy, nine end ureterostomy, 16 loop ureterostomy, and 22 ileal loop (nine were pyeloileal conduits). In 42 cases the urinary diversion had been considered "permanent," and the average duration was almost 8 years. In 16 cases the diversion had been planned as a "temporary" procedure, although interestingly the children had been left with them for almost 3 years on an average (one end ureterostomy, two nephrostomy, 13 loop ureterostomy). Twelve were females, and 46 were males. There were 18 who had only one kidney. Urethral valve obstruction was the most common pathology causing urinary diversion in the first place; eight youngsters had the prune belly syndrome.

Two of these cases (both ileal loops) had undergone their diversions by us many years ago before we turned to primary reconstructive surgery. The remaining 56 patients had their diversions elsewhere and were referred for "undiversion."

The bladder in these patients is usually quite small from long-standing disuse. This precludes satisfactory preoperative assessment of bladder function except to note sensation when the bladder is filled. Usually these youngsters don't know what to do when asked to void at cystogram examination, although they learn how to do so soon postoperatively. We have been careful to avoid "undiversion" on any patient whose problem appeared to be neurogenic bladder. Although some authors[31, 51] have thought that certain long diverted bladders were not satisfactory for refunctionalization, to date we have not found that to be the case. Admittedly some seem to acquire normal capacity and control more quickly than others. Most importantly, small bladders which preoperatively hold only 15 to 20 ml can adapt very soon postoperatively, gaining

Table 1. *Urinary Undiversion in Children*

58 Cases (18 solitary kidney) 12 Girls 46 Boys	4 Nephrostomy 7 Cystostomy 9 End ureterostomy 16 Loop ureterostomy 22 Ileal loop (9 pyeloileal)

normal capacity in a matter of weeks. In two cases where it was uncertain if the external sphincter mechanism was satisfactory, suprapubic cystostomy tube was performed, instructing the patient to fill the bladder several times daily in order to test control and simultaneously increase the bladder capacity. One of these patients had total incontinence, secondary to urethrotomy many years before. The urethra was repaired, continence was restored, and the ileal loop was "undiverted."

Technical Considerations

No two cases have been just alike, and yet there are some generalizations which can be made about these cases. First, they are all long, difficult procedures. Many of these youngsters have diminished renal function, leaving little margin of safety in event of complication. This surgery must be done precisely with respect to blood supply, ureters must be implanted without angulation, and the child must not be left with reflux. In many of the cases simultaneous exposure of the entire urinary tract was needed, i.e., the kidneys, ureters, and bladder. Not infrequently a kidney must be shifted downward to gain adequate ureteral length. In many patients simultaneously a loop ureterostomy was taken down and closed, in order to get length of ureter to reach the bladder. This must be done with great care to the blood supply of the ureter, lest it be devascularized. Ureterostomy can tether the ureter upward, so that there is no slack in the lower ureter to permit reimplantation unless the ureterostomy is mobilized. A number of these cases have been reported previously[10, 20, 24] to illustrate the spectrum of technical maneuvers employed in performed "undiversion." The following two cases are representative:

CASE 3

This 11-year-old boy was referred for undiversion in January 1974 (Figs. 8 and 9). In August 1963 at age 3 months urinary infection occurred; cystography showed massive reflux and hydronephrosis. Suprapubic cystostomy was performed. At age 2 years, September 1965, a cystogram through the suprapubic tube showed continuing reflux. The patient had formed bilateral renal calculi; bilateral nephrolithotomy was performed. In March 1966 an ileal conduit was performed. Following this, his clinical course was much improved, although at age 3½ yrs. a second left nephrolithotomy was required. He was maintained on low dose suppressive antimicrobial therapy initially, but during the 3 years before referral, the urine had been consistently sterile off medication. Simultaneous cystogram and loopogram showed a small bladder, and a satisfactory ileal conduit. The patient could not empty the bladder, but seemed to have normal sensation. At operation valves were resected endoscopically, the loop was tapered and reimplanted with a long submucosal tunnel. I.V.P. 2 weeks postoperatively was satisfactory. Cystography did not show reflux. The patient had frequent urination initially, but at 4 weeks postoperatively developed normal urinary frequency and control, with a bladder capacity of about 350 ml.

COMMENT. This case is anatomically similar to many youngsters who have undergone urinary diversion by ileal loop who might be considered for operation. In most of the ileal conduits reconstruction was performed in this manner.

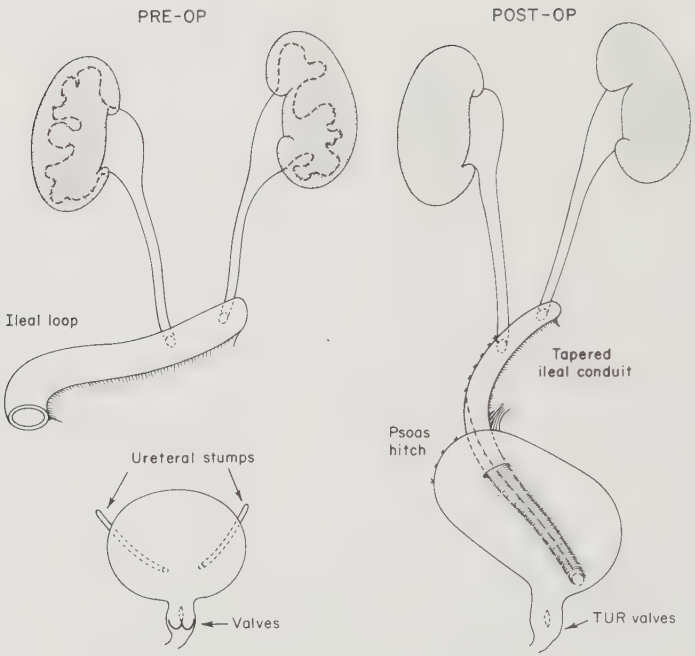

Figure 8. (Case 3) Anatomy before and after repair.

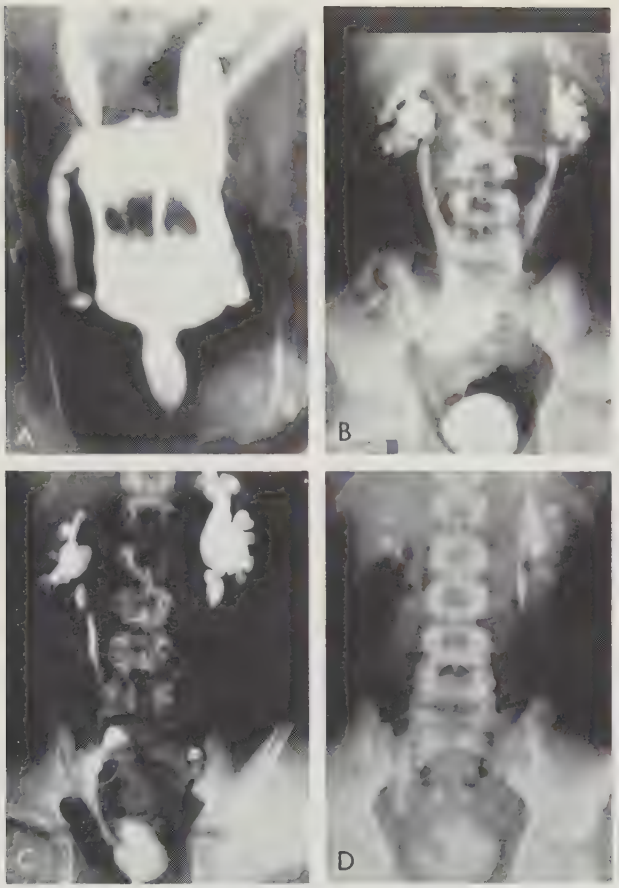

Figure 9. (Case 3) *A*, Cystogram at 3 months through suprapubic tube. Note dilated prostatic urethra (valves) and reflux. *B*, Simultaneous loopogram and cystogram prior to undiversion at age 11 yr. *C*, Retrograde pyelogram 6 mo after reconstruction to outline entire urinary tract. *D*, IVP 1 yr postoperatively. Satisfactory upper tract drainage; normal bladder capacity; no reflux.

Technique of "Undiversion" from Ileal Loop

In Figure 10 are shown the possible reconstructive techniques after ileal loop. We have not seen a case where both ureters were long enough to implant into the bladder. In the majority (17 cases), the ileal loop was tapered and implanted into the bladder with a long tunnel to prevent reflux. Nine of these cases were pyeloileal conduits, with no ureters remaining. In three cases the loop was discarded, implanting one ureter into the bladder; one of these children had only one kidney, and in the other two transureteroureterostomy was performed with the shorter ureter. In a single case upper and lower ureter was usable, and the ileal loop provided the middle third of the ureter.

Use of small bowel as a ureteral substitute is not new. Goodwin[10] reported using the procedure in a variety of circumstances, but did not taper the caliber of the bowel as Swenson[19] did, nor was an antirefluxing anastomosis used. He emphasized joining the conduit low to a fixed part of the bladder to avoid angulation. In children with long life expectancy, we prefer to perform an antirefluxing procedure, although it is technically much more difficult. The caliber of the conduit is tapered about 50 per cent. This enhances peristaltic emptying, reduces its absorptive surface, and allows a nonrefluxing reimplant. From extensive experience with vesicoureteral reflux, we believe than an antirefluxing method must be preferred to one which permits reflux, particularly in young patients who already have in many instances considerable renal damage. Figure 11 shows the technique used for implanting an ileal conduit into the bladder.

CASE 4

This youngster was referred in January 1973 at age 12 years for possible reconstruction (Figs. 12 and 13). At age 9 months he had urinary infection, found to be secondary to ureterocele with bilateral massive hydronephrosis. Initial surgery consisted of incision of the ureterocele, with suprapubic cystostomy; later there was a Y-V revision of the bladder neck at age 2 years. At age 3 years bilateral end ureterostomies were performed. Study on admission showed a small bladder, with residual ureteral stumps bilaterally, and duplex collecting systems. There was good renal parenchyma remaining in only the upper pole of the left kidney. There was no drainage from the ureterostomy stomas on the right side, i.e., chronic infection had totally destroyed that kidney.

Operation included right nephroureterectomy, removal of the lower pole ureter on the left, with preservation of the blood supply of the adjacent upper pole ureter, lower pole pyeloureterostomy, repair of the ureterocele defect in the trigone, excision of three ureteral stumps, and ureteral reimplantation. The procedure was done with wide transabdominal exposure and lasted for 9 hours. The patient did well postoperatively, with consistently sterile urine. Intravenous pyelogram 14 months later was satisfactory. His serum creatinine is 0.7 mg per cent, BUN 16 mg per cent. The average value of two postoperative creatinine clearances is 74 L absolute, reflecting hypertrophy of the left upper pole in response to loss of the right kidney function as an infant.

Comment. Refunctionalization of this youngster's urinary tract has resulted in sterilization of his urine, which had always been infected previously. Cystogram 1 year after reconstruction showed mini-

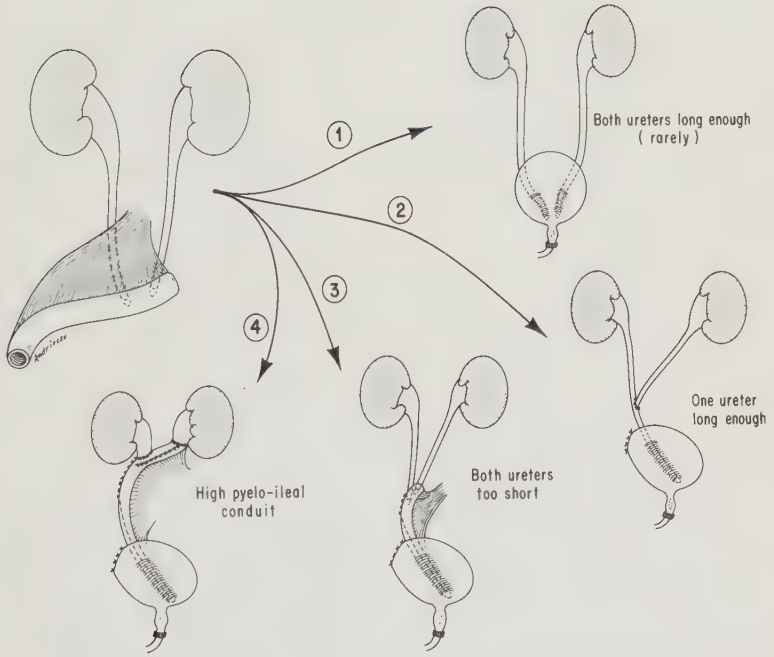

Figure 10. Alternative reconstructive technique following ileal loop.

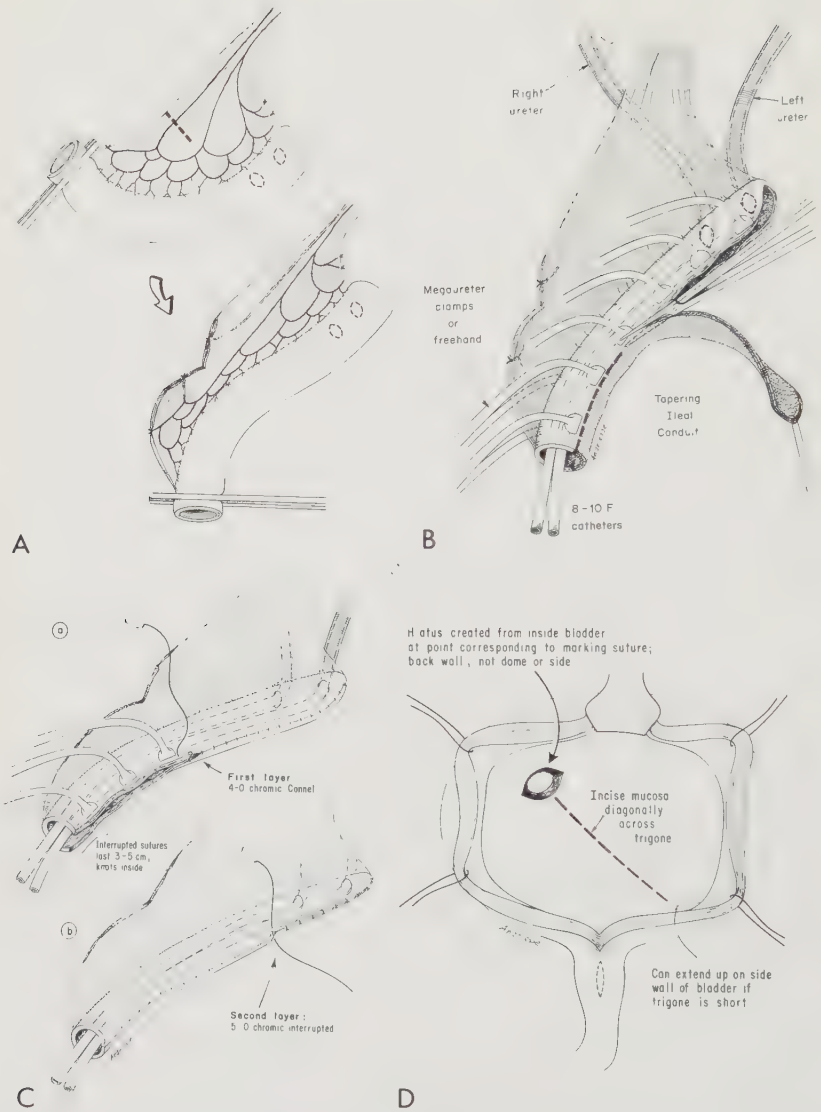
A
Right ureter
Left ureter
Megaureter clamps or freehand
Tapering Ileal Conduit
8-10 F catheters
B
First layer 4-0 chromic Connel
Interrupted sutures last 3-5 cm, knots inside
Second layer: 5-0 chromic interrupted
C
Hiatus created from inside bladder at point corresponding to marking suture; back wall, not dome or side
Incise mucosa diagonally across trigone
Can extend up on side wall of bladder if trigone is short
D

Figure 11. *A*, Mesentery is opened to straighten conduit. *B*, Caliber is tapered. *C*, Two-layer closure with chromic catgut. Distal part of closure is made with interrupted sutures in order to be able to trim conduit later to suitable length. *D*, The mucosal tunnel is created by incising mucosa to make a tunnel because bluntly tunneling beneath the mucosa is frequently impossible in these bladders.

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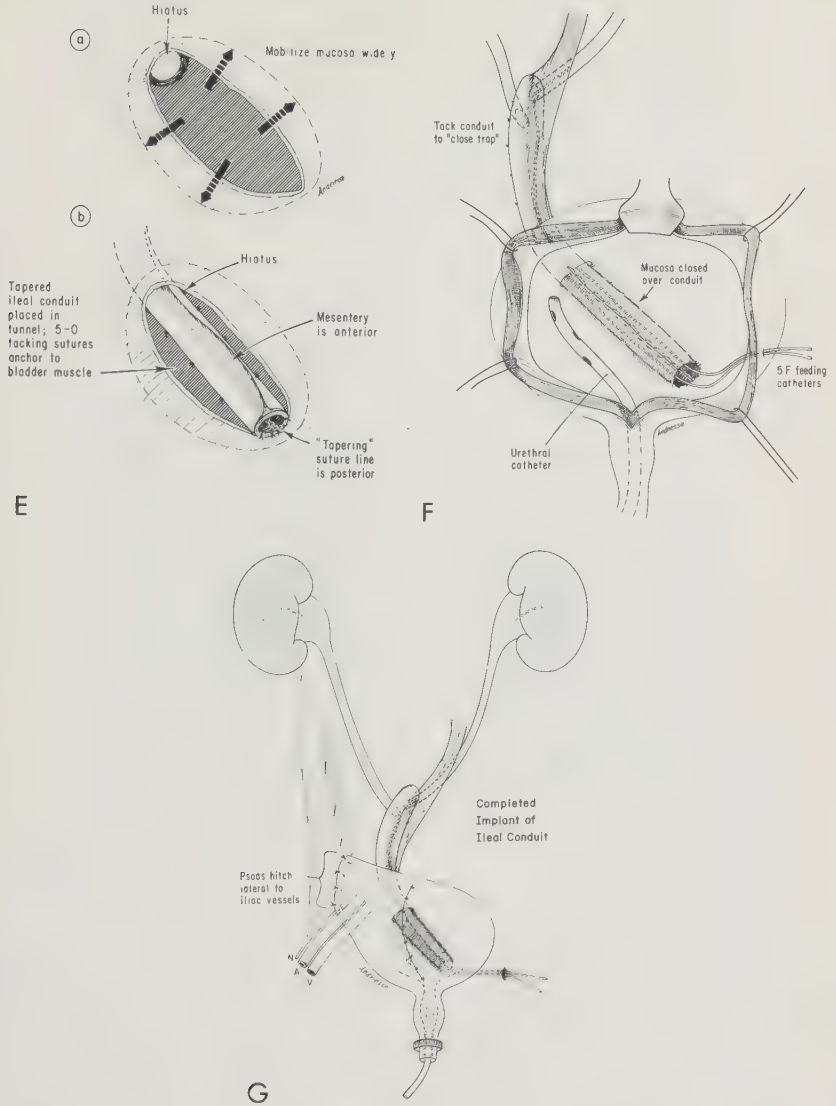

Figure 11 *Continued.* *E*, Mucosa is mobilized widely, conduit is placed in it, with the tapering suture line posteriorly. Excess fat is trimmed from the mesentery, which lies anteriorly, and excess length of conduit discarded. *F*, Soft drainage catheters are passed up the ureters for temporary decompression for 10 to 12 days. *G*, Completed implant with anchoring of bladder lateral to point of entry of conduit to immobilize it, which will protect against angulation when the bladder fills. This helps achieve adequate tunnel length of 3 to 5 cm in very small contracted bladders.

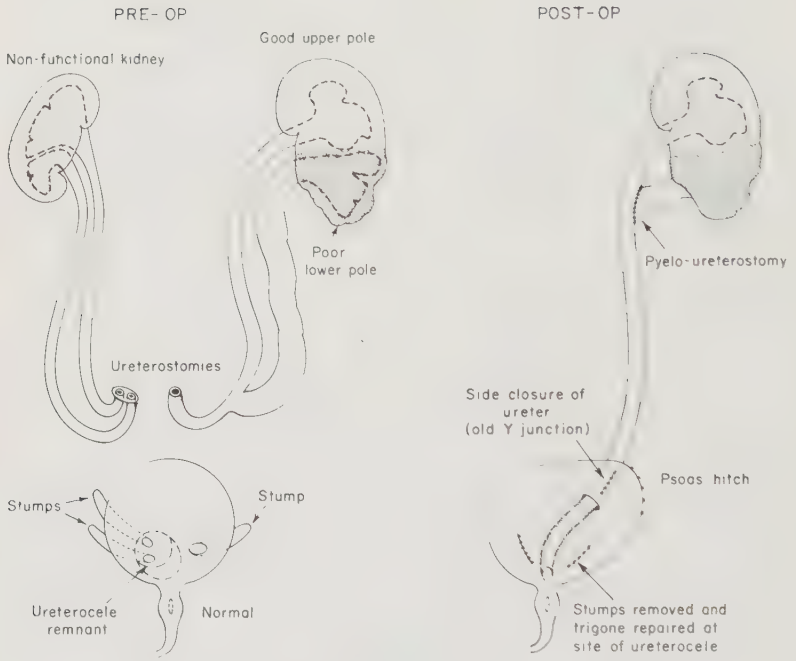

Figure 12. (Case 4) Anatomy before and after repair.

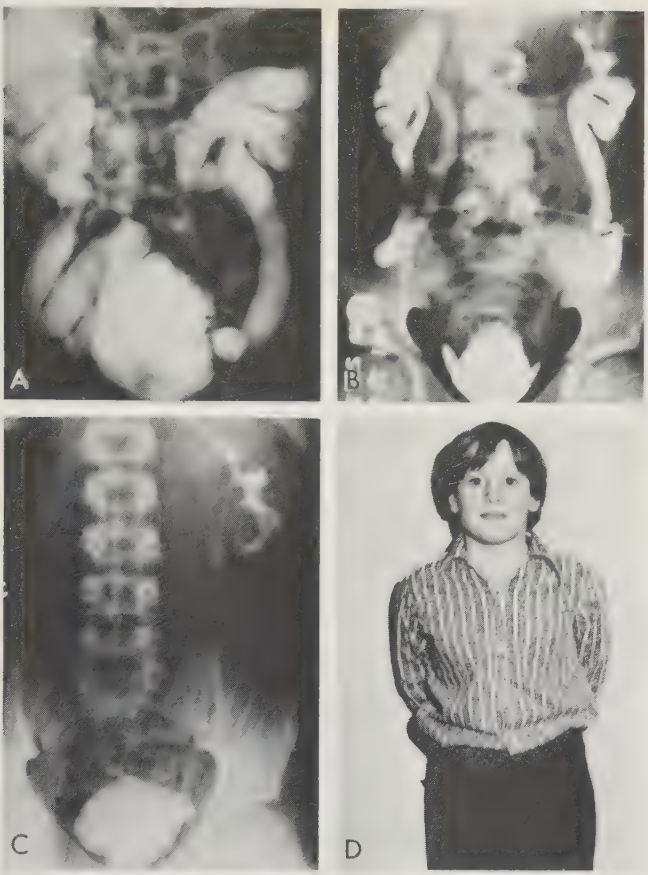

Figure 13. (Case 4) *A*, Cystogram at age 9 months with bilateral massive hydronephrosis caused by ureterocele. *B*, Preoperative cystogram and ureterograms before reconstruction, showing small bladder, residual ureteral stumps, and tortuous ureters bilaterally. *C*, IVP 14 months postoperatively. *D*, The patient at age 13 yr.

mal vesicoureteral reflux, which later disappeared. There has been a dramatic change in his personality. Formerly a combative, ill adjusted underachiever in school, who spoke of suicide if he had to continue with a bag on his side, he has undergone a complete reversal. He seems happy, is doing well in school, and requires no medication.

CONCLUSION

The indications for urinary diversion have decreased in the past few years since other alternatives have developed. If permanent diversion is required, as it will continue to be in some, it should be by a method which is not prone to give further upper tract deterioration. We believe that long-term observation will show the nonrefluxing colon conduit to be better than the ileal loop, although 15 years must pass to be certain of

that. Clearly the bladder should not be removed, as it was so often in the past, to treat actual or possible pyocystis which can occur in the defunctionalized bladder. If it does appear, it can be managed by antibiotic washouts. Future developments may make possible the use of some of these bladders, even in neurogenic cases.

There are many children living with urinary diversions who should be reassessed with an eye to possible "undiversion," provided there is no reason to suspect a bladder innervation problem, and provided the continence mechanism is intact. The magnitude of "undiversion" should not be underestimated, however. It is a formidable undertaking, often taking 6 to 8 hours or longer and leaving a little margin of safety for the patient in the event of technical error. This type of surgery should be reserved, in my opinion, to those centers with expert pediatric anesthesia and where surgeons have large experience performing major reconstructive urologic operations on young patients.

REFERENCES

1. Allen, T. D., Glenn, J. F., Hendren, W. H., et al.: Management of the severely obstructed urinary tract in the pediatric patient—a panel discussion. J. Ped. Surg., 7:706, 1972.
2. Bennett, A. H.: Exstrophy of the bladder treated by ureterosigmoidostomy: Long term evaluation. Urology, 2:165, 1973.
3. Bischoff, P.: Megaureter. Br. J. Urol., *29*:416, 1957.
4. Bricker, E. M.: Bladder substitution after pelvic evisceration. SURG. CLIN. N. AM., *30*:1511, 1950.
5. Chisholm, T. C.: Exstrophy of the urinary bladder. *In* Mustard, W. T., et al. (eds.): Pediatric Surgery, 2nd ed., Vol. 2, Chicago, Yearbook Medical Publishers, 1969, Ch. 73.
6. Delgado, G. E., and Muecke, E. C.: Evaluation of 80 cases of ileal conduits in children: Indication, complication and results. J. Urol., *109*:311, 1973.
7. Dretler, S. P., Hendren, W. H., and Leadbetter, W. F.: Urinary tract reconstruction following ileal conduit diversion. J. Urol., *109*:217, 1973.
8. Durham-Smith, E.: Followup studies on 150 ileal conduits in children. J. Ped. Surg., 7:1, 1972.
9. Fisher, J. H.: Exstrophy of the bladder. J. Ped. Surg., 4:620, 1969.
10. Goodwin, W. E., Winter, C. C., and Turner, R. D.: Replacement of the ureter by small intestine: Clinical application and results of "ileal ureter." J. Urol., *81*:406, 1959.
11. Gregoir, W.: Le traitement chirurgical du reflux vesico-ureteral congenital. Acta Chir. Belgica, 4:431, 1964.
12. Gross, R. E.: Urinary and fecal incontinence of neurogenic origin. *In* Gross, R. E.: The Surgery of Infancy and Childhood. Philadelphia, W. B. Saunders Co., 1953, Ch. 56.
13. Hendren, W. H.: Ureteral reimplantation in children. J. Ped. Surg., 3:649, 1968.
14. Hendren, W. H.: Operative repair of megaureter in children. J. Urol., *101*:491, 1969.
15. Hendren, W. H.: A new approach to infants with severe obstructive uropathy: Early complete reconstruction. J. Ped. Surg., 5:184, 1970.
16. Hendren, W. H.: Posterior urethral valves in boys: A broad clinical spectrum. J. Urol., *106*:298, 1971.
17. Hendren, W. H.: Restoration of function in the severely decompensated ureter. *In* Johnston, J. H., and Scholtmeijer, R. J. (eds.): Problems in Paediatric Urology. Amsterdam, Excerpta Medica, 1972, pp. 1–56.
18. Hendren, W. H.: Reconstruction of previously diverted urinary tracts in children. J. Ped. Surg., 8:135, 1973.
19. Hendren, W. H.: Reoperation for the failed ureteral reimplantation. J. Urol., *111*:403, 1974.
20. Hendren, W. H.: Urinary tract refunctionalization after prior diversion in children. Ann. Surg., *180*:494, 1974.
21. Hendren, W. H.: Complications of megaureter repair in children. J. Urol., *113*:238, 1975.
22. Hendren, W. H.: Nonrefluxing colon conduit for temporary or permanent urinary diversion in children. J. Ped. Surg., *10*:381, 1975.
23. Hendren, W. H.: Refunctionalizing the urinary tract after prior diversion. Contemp. Surg., 7:63, 1975.

24. Hendren, W. H.: Reconstruction ("undiversion") of the diverted urinary tract. Hosp. Pract., *11*:70, 1976.
25. Hendren, W. H.: Exstrophy of the bladder: An alternative method of management. J. Urol., in press 1976.
26. Hutch, J. A., Miller, E. R., and Hinman, F., Jr.: Vesicoureteral reflux: Role in pyelonephritis. Am. J. Med., *34*:338, 1963.
27. Johnston, J. H.: Temporary cutaneous ureterostomy in the management of advanced congenital urinary obstruction. Arch. Dis. Child., *38*:161, 1963.
28. Johnston, J. H.: Reconstructive surgery of megaureter in childhood. Br. J. Urol., *39*:17, 1967.
29. Leape, L. L., and Holder, T. M.: Temporary tubeless urinary diversion in children. J. Ped. Surg., *5*:288, 1970.
30. Lome, L. G., and Williams, D. I.: Urinary reconstruction following temporary cutaneous diversion in children. J. Urol., *108*:162, 1972.
31. Lome, L. G., Howat, J. M., and Williams, D. I.: The temporary defunctionalized bladder in children. J. Urol., *107*:469, 1972.
32. Marshall, V. F., and Muecke, E. C.: Functional closure of typical exstrophy of the bladder. J. Urol., *104*:205, 1970.
33. Mathisen, W.: A new method for uretero-intestinal anastomosis. Surg. Gynec. Obstet., *96*:255, 1953.
34. McGovern, J. H., and Marshall, V. F.: Reimplantation of ureters in children. Surg. Gynec. Obstet., *114*:143, 1962.
35. McLaughlin, A. P., III, Leadbetter, W. F., and Pfister, R. C.: Reconstructive surgery of primary megaloureter. J. Urol., *106*:186, 1971.
36. Megalli, M., and Lattimer, J. K.: Review of the management of 140 cases of exstrophy of the bladder. J. Urol., *109*:246, 1973.
37. Middleton, A. W., and Hendren, W. H.: Ileal conduits in children at the Massachusetts General Hospital from 1955 to 1970. J. Urol., in press 1976.
38. Mogg, R. A.: Some observations on urinary diversion. Ann. Roy. Coll. Surg. Engl., *46*:251, 1970.
39. Paquin, A. H., Jr.: Considerations for the management of some complex problems for ureterovesical anastomosis. Surg. Gynec. Obstet., *118*:75, 1964.
40. Perlmutter, A. D., and Patil, J.: Loop cutaneous ureterostomy in infants and young children: Late results in 32 cases. J. Urol., *107*:655, 1972.
41. Pitts, W. R., Jr., and Muecke, E. C.: Congenital megaloureter: a review of 80 patients. J. Urol., *111*:468, 1974.
42. Politano, V. A., and Leadbetter, W. F.: An operative technique for the correction of vesicoureteral reflux. J. Urol., *79*:932, 1958.
43. Retik, A. B., Perlmutter, A. D., and Gross, R. E.: Cutaneous ureteroileostomy in children. N. Eng. J. Med., *277*:217, 1967.
44. Richie, J. P.: Intestinal loop urinary diversion in children. J. Urol., *111*:687, 1974.
45. Richie, J. P., Skinner, D. G., and Waisman, J.: The effect of reflux on the development of pyelonephritis in urinary diversion: An experimental study. J. Surg. Res., *16*:256, 1974.
46. Richie, J. P., and Skinner, D. G.: Urinary diversion: The physiological rationale for nonrefluxing colonic conduits. Br. J. Urol., *47*:269, 1975.
47. Scott, F. B., Bradley, W. E., and Timm, G.: Use of an implantable artificial sphincter in the treatment of urinary incontinence. J. Urol., *112*:75, 1974.
48. Spence, H. M.: Ureterosigmoidostomy for extrophy of the bladder. Results in a personal series of 31 cases. Br. J. Urol., *38*:36, 1966.
49. Swenson, O., Fisher, J. H., and Cendron, J.: Megaloureter: Investigation as to the cause and report on the results of newer forms of treatment. Surgery, *40*:223, 1956.
50. Tanagho, E. A.: Ureteral tailoring. J. Urol., *106*:194, 1971.
51. Tanagho, E. A.: Congenitally obstructed bladders: Fate after prolonged defunctionalization. J. Urol., *111*:102. 1974.
52. Williams, D. I., and Keeton, J. E.: Further progress with reconstruction of the exstrophied bladder. Br. J. Surg., *60*:203, 1973.

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Recent Advances in Cardiac Surgery in the Young Infant

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Over the past several years, better understanding of the pathophysiology of neonatal illnesses has improved the management of sick newborns and infants, especially in the area of pulmonary care. Simultaneous advances in surgical techniques such as optical magnification, microsurgery, and deep hypothermia have made cardiac surgery in infants easier and safer. Because of these developments, many operations that once had a very high mortality rate in young infants can now be performed safely. Although the most dramatic recent changes have been in the area of corrective heart surgery during infancy, we will discuss first the recent use in premature infants of an operation that was formerly performed almost exclusively in older children, closure of a patent ductus arteriosus (PDA).

PATENT DUCTUS ARTERIOSUS IN PREMATURE INFANTS

As the postnatal care of premature infants has improved, the survival rate has risen from less than half in the mid-1960's to four-fifths or more in recent years.[42] About 15 per cent of premature infants have a PDA and about 60 per cent have idiopathic respiratory distress syndrome (IRDS).[9] Infants with IRDS are more likely to have PDA than are those without IRDS.[7] Because the PDA may close spontaneously, surgical interruption was not considered to be indicated for these infants prior to the late 1960's. As survival rates improved, it became apparent that some premature infants with IRDS died from congestive heart failure (CHF) due to the large left-to-right shunt of a PDA. Since then, sev-

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eral reports have indicated that surgical intervention may dramatically alter the course of some prematures with PDA.[9, 21, 42]

Because of differences in clinical course and response to surgery, premature infants with PDA should be separated into two groups, those with IRDS and those without.

In patients without IRDS, the appearance of CHF is delayed until the pulmonary artery pressure falls after the first several days or weeks of life. At that time, most patients develop the systolic murmur, cardiomegaly, and increasing arterial pulse pressure typical of PDA. Most of these patients also have tachypnea, tachycardia, rales, hepatomegaly, and increased pulmonary vascularity on chest roentgenogram. Episodic bradycardia and episodic apnea usually occur. The indication for surgical interruption of the PDA in infants without IRDS is intractable CHF after a trial of maximal medical therapy, that is, digitalis, diuretics, and ventilatory assistance. The operation performed is ligation of the ductus arteriosus. The procedure is rapidly performed, seldom taking more than 15 minutes, and is safe (no operative deaths have occurred in several series).[9, 21, 42] The results of PDA ligation are very good in patients without IRDS. Most have immediate improvement in their clinical status with disappearance of CHF, cardiomegaly, and respirator requirements, and rapid weight gain. A few may develop retrolental fibroplasia or neurologic and developmental abnormalities, complications of their immaturity rather than of the PDA.[9]

Premature infants with IRDS, on the other hand, maintain very high pulmonary artery resistance and pressure during their early days of life when the IRDS is most severe. At this time, the ductus arteriosus is usually open, but because the systemic and pulmonary resistances are equal, there is either no net shunt or it is right-to-left. As IRDS resolves, pulmonary artery resistance and pressure fall and the net shunt becomes left-to-right. The clinical course of infants with IRDS is, therefore, characterized by initial improvement in the IRDS, manifested by decreasing oxygen requirement, P_{CO_2} level, and respiratory rate, and clearer lung fields. As left-to-right shunting through the PDA appears and increases, the IRDS seems to get worse again with increasing oxygen requirement, increased P_{CO_2} level, increased respiratory rate and need for ventilatory assistance, tachycardia, and increasing vascularity of the lungs on roentgenogram. Episodes of bradycardia and apnea become more frequent. These patients usually do not develop the massive cardiomegaly seen in infants in CHF due to PDA without IRDS.[9]

Indications for surgical closure of the ductus in infants with IRDS are not clearly established. The deterioration that follows initial recovery can be treated with intensive medical measures, reserving surgery for severely ill or moribund patients. A more aggressive approach is to ligate the PDA as soon as the presence of a large left-to-right shunt through the PDA is confirmed. The operation performed in infants with IRDS is technically the same as in those without IRDS, ligation of the ductus arteriosus. However, the results are usually not as good as in patients without IRDS. Although most patients improve after surgery, some die of progressive lung disease or of complications such as sepsis and necrotizing enterocolitis. Approximately half of the surgically

treated premature infants with PDA and IRDS leave the hospital, but it has become apparent on late follow up[3] that many of these infants have severe neurologic or pulmonary sequelae, ranging from gross mental retardation to bronchopulmonary dysplasia and repeated lung infections.

The likelihood of survival after surgical ligation of the patent ductus arteriosus is related to: (1) the size of the patient, with an 80 per cent survival rate in infants over 1000 gm. and 30 per cent survival under 1000 gm.;[32] (2) the severity of the IRDS, those infants having the most severe type of IRDS being less likely to survive; and (3) the point in the course of the IRDS at which surgical ligation is undertaken. Recent reports have suggested that earlier ligation of the ductus decreases morbidity and mortality.[21, 42]

The issue of PDA ligation in premature infants is not settled. A major difficulty arises in deciding when maximal medical management has failed, complicated by the knowledge that most PDA's will eventually close spontaneously. It is known that prolonged left-to-right shunting may leave premature infants with severe chronic pulmonary disease. Early division of the PDA may reverse: (1) the prolonged hypoxemia associated with CHF in the infant with IRDS that may cause cerebral damage; (2) the necessity for prolonged high inspired oxygen tension and high ventilatory pressures, both of which are related to chronic lung damage; and (3) the inadequate weight gain associated with prolonged congestive heart failure.

PALLIATION VERSUS CORRECTION IN INFANCY

The first operation for congenital heart disease was corrective: ligation of a PDA by Robert Gross in 1938.[17] Palliative surgery began with the operation for blue babies that gave enormous impetus to surgery for congenital heart disease: subclavian-to-pulmonary artery anastomosis, reported by Alfred Blalock and Helen Taussig in 1945.[6] Other procedures followed: descending aorta-to left pulmonary artery anastomosis (Potts, 1946),[31] pulmonary artery band (Muller and Dammann, 1952),[29] superior vena cava to right pulmonary artery anastomosis (Glenn, 1958),[15] ascending aorta to right pulmonary artery anastomosis (Waterston, 1962).[41]

Unfortunately, many late complications have been associated with palliative procedures, some of which preclude corrective surgery. Systemic to pulmonary artery anastomoses have been associated with chronic CHF with later development of pulmonary vascular obstructive disease (PVOD),[4] kinking of a pulmonary artery that can produce selective flow to one lung resulting in PVOD in that lung and hypoplasia of the pulmonary vessels in the other;[38] and a higher mortality at corrective operation due to technical difficulties imposed by the previous operation.[10] A pulmonary artery band (PAB) placed to reduce pulmonary blood flow in children with excessive flow may be too loose, resulting in chronic CHF and later development of PVOD; it may be too tight, leading to cyanosis and polycythemia; a branch pulmonary artery may be ob-

structed by a distally placed band; muscular subaortic or subpulmonary obstruction may develop; the band can erode through the wall of the pulmonary artery; the pulmonary valve may become permanently deformed; and a slightly higher mortality rate has been reported when corrective operation is undertaken when PAB is present than when it is not.[16]

Routine corrective surgery in infants has been made possible by two converging lines of investigation: hypothermia and cardiopulmonary bypass. Bigelow reported investigations with hypothermia and circulatory arrest in 1950 that led to the first repair of an atrial septal defect under direct vision by F. John Lewis in 1953.[24] The next year, John Gibbon successfully carried out an intracardiac operation using the pump oxygenator he had been developing in the laboratory over two decades.[12] By 1955, Lillehei was able to report a series of complex lesions, including tetralogy of Fallot, repaired first with controlled cross-circulation and later with cardiopulmonary bypass using a bubble oxygenator.[25]

Throughout the 1950's and early 1960's techniques of bypass and intracardiac operations were continually refined. Nevertheless, mortality remained high in infants and small children, so at young ages, palliative surgery was carried out with a view toward corrective operation at a later time.

In the early 1960's, Japanese surgeons successfully combined the techniques of deep hypothermia and circulatory arrest, later adding cardiopulmonary bypass, to repair intracardiac lesions in infants; the results were very good.[19, 20] The usefulness of hypothermic arrest for infant surgery was brought to the attention of the Western world mainly by Merendino[28] and Barrett-Boyes.[1]

We now use a modification of the technique described by Hikasa and his co-workers.[19] Arterial and central venous monitoring cannulas, a Foley catheter, rectal, esophageal, and nasopharyngeal temperature probes, and electrocardiograph electrodes are placed while surface cooling is begun with ice bags placed on the trunk and head. When catheters and probes have been positioned, the child is placed in a plastic bag, then into a tub containing a small amount of tap water and is packed in ice (Fig. 1). When the rectal temperature reaches 25° C, the child is removed from the tub, his chest is opened, and an aortic and right atrial cannula are connected to a pump oxygenator. The infant is placed on cardiopulmonary bypass with a cold (5–10° C) perfusate until the nasopharyngeal temperature is below 20° C. The aorta is cross-clamped, the pump is stopped, and the atrial cannula is removed after the patient's blood volume has drained into the pump reservoir. The intracardiac procedure is then carried out in a totally motionless, flaccid heart with no venous return to obscure the small structures being repaired. After correction has been completed, the heart is filled with saline, the right atrial cannula is replaced, and a small incision is made in the anterior aorta as an air vent. The pump is started and the aortic cross-clamp is removed. Rewarming is then carried out on the pump, maintaining a temperature difference between the perfusate and the nasopharyngeal temperature of no higher than 10° C. When the rectal temperature has reached 33–34° C, cardiopulmonary bypass is stopped and rewarming is completed with a warming mattress.

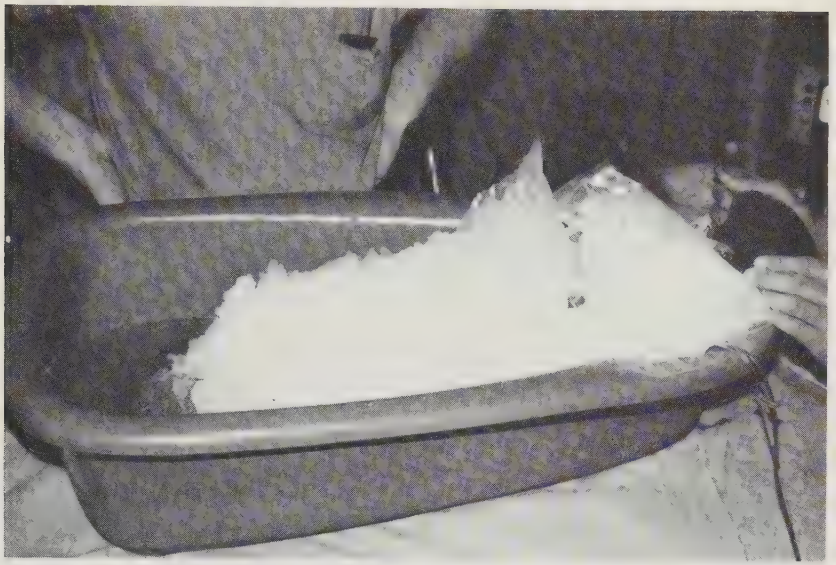

Figure 1. After intubations and cannulations, the infant is placed in a plastic bag, then into a tub with tap water and packed in ice. See text.

The decisive factors in determining whether a palliative or a corrective operation should be performed are mortality and morbidity. The procedure that results in the survival of the greatest number of children with the fewest long-term complications is the procedure of choice. Less crucial factors in favor of initial corrective operation are the avoidance of the psychological stresses on the family and patient that arise from the knowledge that a heart defect is still present and that a second operative procedure will be necessary.[26] The retarded growth and development patterns often associated with severe congenital heart disease are also minimized or avoided by initial corrective operation.

Our early results with corrective cardiac surgery in infants using deep hypothermic circulatory arrest have been favorable,[8, 35] so our policy now is to correct at any age all lesions that are correctable, and palliate only those lesions for which no corrective operation is available or for which corrective operation is suitable only in older children. The rationale for choosing correction over palliation for many of the commonest congenital heart lesions requiring surgery in infants will now be discussed, comparing mortality of palliative operations with that of corrective operations.

Ventricular Septal Defect (VSD)

Infants with large VSDs have a left-to-right shunt that may produce CHF. The CHF usually responds to medical management, but if it does not, surgical intervention is indicated. The choice is between PAB and closing the VSD (Fig. 2). The mortality rate of PAB for isolated VSDs in infants under 3 months of age varies from 5 to 30 per cent.[22] To this must be added the 3 to 5 per cent mortality of later VSD closure with removal of PAB.[14]

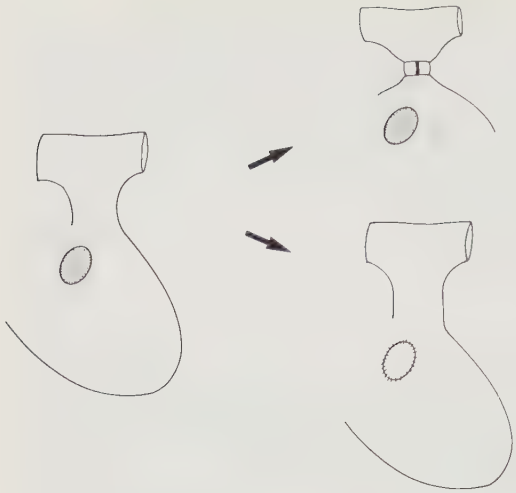

Figure 2. Alternative methods of treating large ventricular septal defect with refractory congestive heart failure are pulmonary artery band and closure of ventricular septal defect.

In infants over 3 months of age, initial repair of the VSD is clearly safer than two-stage correction. None of our 18 patients died, an experience similar to that of others.[40] Under the age of 3 months, three of 15 patients died, and two of these deaths were preventable. The third death occurred in a severely ill patient with advanced bilateral pulmonary disease; this child should have undergone PAB. With proper selection of patients, excluding those with severe lung disease, death after VSD repair should occur rarely.

Therefore, our current policy is to do initial repair of VSD at all ages whenever an operation is indicated. Infants with severe pulmonary disease should undergo PAB.

Satisfactory closure of VSDs in infants can be achieved in most cases through the right atrium by retracting the tricuspid valve. The exceptions are subpulmonary VSD which requires right ventriculotomy and multiple VSDs which may require left apical ventriculotomy. One of our patients had multiple VSDs that could not be closed through the right atrial approach. He had a single patch placed over the clearly visible left ventricular aspect of the VSD through an apical left ventriculotomy. In one patient early in our experience a large endocardial cushion type VSD was incompletely closed deliberately to avoid heart block; this patient later required PAB. We use knitted Dacron for patch material.

The coexistence of VSD with coarctation of the aorta in infants with congestive heart failure is not uncommon. Our approach to this problem is initially to repair the coarctation. In the past, this has been accomplished by resection and primary anastomosis; however, because the incidence of recurrence is about 20 per cent when repair is carried out in infancy, we are now considering using an onlay patch repair without resection of the coarctation.[32] If after repair of the coarctation the VSD continues to be hemodynamically significant with severe congestive heart failure, we do not band the pulmonary artery but repair the VSD as described above as soon as necessary, sometimes within 24 hours.

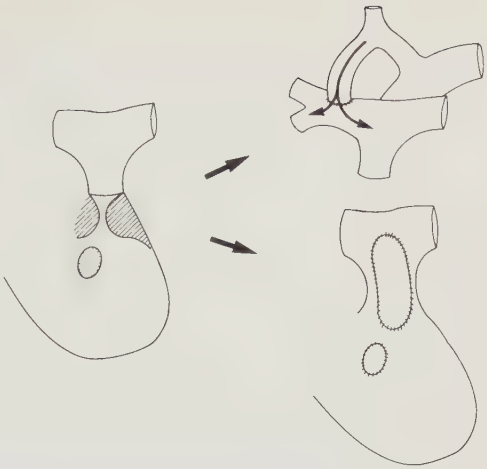

Figure 3. Surgical treatment of tetralogy of Fallot in infancy can be palliative shunt (Blalock-Taussig shown here) or correction (closure of ventricular septal defect and patching the pulmonary outflow tract).

Tetralogy of Fallot (TOF)

Surgery is indicated for infants with TOF who have severe hypoxemia, have documented hypoxemia spells, or are found at cardiac catheterization to have suprasystemic right ventricular pressure due to tricuspid leaflet tissue partially obstructing the VSD (Fig. 3). Palliative aorta-to-right pulmonary artery anastomosis in infants with TOF is associated with a mortality rate of about 20 per cent, ranging from 12[23] to 50 per cent.[2] Later correction with closure of the shunt has a mortality rate between 8 and 60 per cent.[34] The combined mortality of two-stage repair, therefore, is at least 20 per cent, but may be over 50 per cent.

In our group of 23 infants who underwent initial repair, ten were under 3 months of age and only one died (Fig. 4). The death was due to

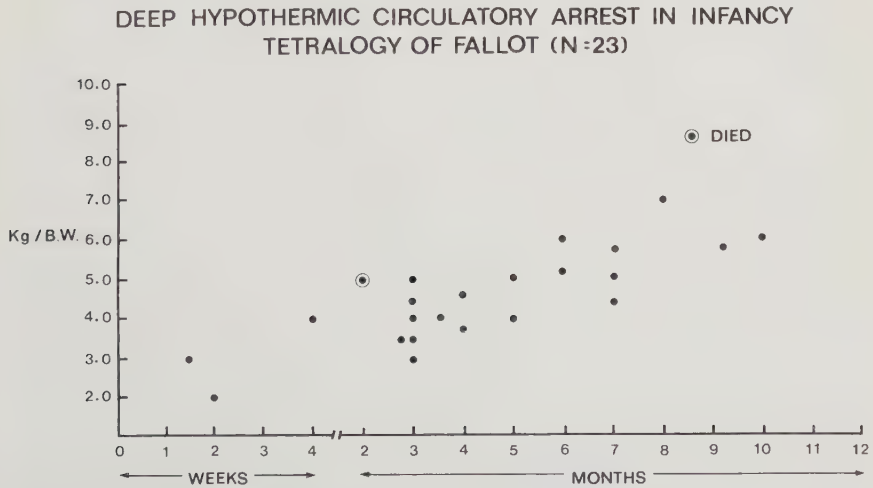

Figure 4. Weight plotted against age of our group of infants who have undergone corrective operation for tetralogy of Fallot.

necrotizing enterocolitis that, in retrospect, was probably present preoperatively. No patient under the age of 3 months required reoperation for a residual lesion. Two older infants did not have an outflow patch placed across the pulmonary annulus at the initial operation, and required reoperation for residual pulmonary stenosis with right ventricular outflow aneurysm. A third patient with a right ventricle-pulmonary artery pressure difference of 50 mm Hg may later require a second procedure for relief of pulmonary stenosis. Although no long-term follow-up is yet available, the early follow-up results appear promising and the very low mortality rate is strongly in favor of corrective operations for these infants.

Our current policy for symptomatic infants with TOF with unambiguous anatomy on angiocardiogram is to do an initial corrective operation. Palliative anastomoses are done, however, in patients with pulmonary atresia, severe hypoplasia of the pulmonary arteries, or anomalous anterior descending artery from the right coronary. Only one infant with TOF has been denied initial corrective operation on the basis of these contraindications in the past 2½ years.

The major technical consideration in this group of infants is related to the right ventricular outflow tract. Since these infants are the subgroup of TOF that presents earliest in life, they have the severest malformations. Annular hypoplasia is a constant finding, and all patients require a transannular outflow patch. The three patients in whom this was not carried out had residual outflow gradients and two have already been reoperated for placement of an outflow patch. The requirement for a transannular patch in all patients is the reason we use palliative operations in infants in whom the anterior descending artery crosses the pulmonary infundibulum. Knitted Dacron is used to patch the VSD and pericardium is used to enlarge the outflow tract.

Transposition of the Great Arteries (TGA)

Most of these patients have severe cyanosis which appears in the first few days or weeks of life. At cardiac catheterization, balloon atrioseptostomy is performed routinely and results in improvement of arterial O_2 saturation in most patients. However, in our institution, 25 per cent failed to improve after balloon septostomy, and in 50 per cent, severe cyanosis reappeared within 5 months (mean age at balloon septostomy—1 week) (Buckley, L. P.: Personal communication). When O_2 saturation is below 60 per cent or metabolic acidosis is present, it is possible to do either a palliative (Blalock-Hanlon septectomy), or a corrective (Mustard) operation (Fig. 5). Mortality rate after the Blalock-Hanlon procedure is from 5 to 16 per cent.[18]

In our group of nine patients under 3 months of age who underwent corrective operation, the only death was that of a child who was 5 days of age at the time of operation. The death occurred in the hospital a month after operation on the day of planned discharge. In the group of 15 patients over the age of 3 months, there were three deaths, two of which occurred in patients with both TGA and VSD. Despite these favorable mortality rates, obstruction of the superior vena cava was a problem in early infancy, two patients requiring a side-to-side cavopul-

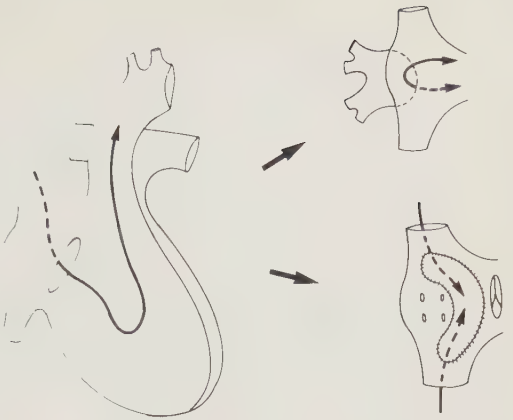

Figure 5. Surgical treatment of transposition of the great arteries may include Blalock-Hanlon septectomy and correction by interatrial baffle (Mustard procedure).

monary anastomosis to decompress the obstructed cava.[8] Both patients have done well since. In recent months we have used a baffle with a pantaloon configuration, suggested by Professor A. G. Brom (personal communication), and have seen no venous obstruction since.

Our policy now is to treat all patients initially with balloon atrioseptostomy. Because of the well-documented propensity for the development of pulmonary vascular obstructive disease, elective corrective operation is carried out at the age of 1 year for patients with intact ventricular septum. Those with VSD are recatheterized at the age of 6 months. If the pulmonary artery-to-systemic artery pressure ratio is greater than 0.75, Mustard operation and closure of VSD is undertaken at that time. Those with a ratio lower than 0.75 undergo elective Mustard operation at 1 year.

If deterioration of clinical status requires operation before the elective age, Mustard operation (and closure of VSD if present) is carried out in patients over 1 month of age. In patients with intact ventricular septum under 1 month, Blalock-Hanlon septectomy is carried out. Patients with VSD who develop CHF under the age of 1 month undergo PAB, and those over 1 month undergo Mustard operation with closure of VSD. A few patients respond poorly to Blalock-Hanlon septectomy even under 1 month; such patients should undergo Mustard operation.

Several technical maneuvers are useful in this group of patients. In the smallest infants, we prefer to use pericardium for the baffle because of its suppleness and ease of handling inside the small atrium. However, in older infants, we frequently use a knitted Dacron baffle and use pericardium to augment the size of the functional left atrium. Considerable advantage can be gained in the construction of the posterior suture line by opening the coronary sinus and sewing the posterior edge of the patch to the pulmonary venous margin of the open coronary sinus, as suggested by Professor Äke Senning (personal communication).

Total Anomalous Pulmonary Venous Connection (TAPVC)

Patients with TAPVC may present early in infancy with severe cyanosis, marked respiratory distress, and signs of pulmonary edema

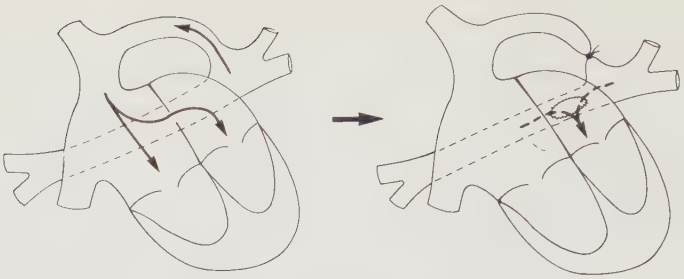

Figure 6. Total anomalous pulmonary venous connection is corrected by diverting common pulmonary vein drainage into the left atrium. In the supracardiac type, the ascending vein connecting the common pulmonary vein to a systemic vein is ligated and an anastomosis created between the common pulmonary vein and the posterior wall of the left atrium.

due to obstruction of pulmonary venous drainage. Once the diagnosis is established, no palliative operation is available, so all must undergo initial correction (Fig. 6). Because of the rapid deterioration often seen in infants with pulmonary venous obstruction, urgent operation should be carried out soon after cardiac catheterization.

Of the 11 infants who have undergone correction of TAPVC, five were less than a month old, and the youngest patient to survive surgery was 36 hours old. Three patients died, all in severe low output state. Six patients had supracardiac connection, two intracardiac to the coronary sinus, and three infradiaphragmatic.

Correction of the coronary sinus type of TAPVC is accomplished by fenestration of the coronary sinus to the base of the left atrial appendage.[39] The coronary sinus orifice is then closed with sutures, avoiding the tail of the atrioventricular node. Thus, all coronary sinus blood drains to the left atrium, all interatrial communications are closed, and a small right-to-left shunt (coronary sinus return) remains.

For both infra- and supracardiac types, the communicating ascending or descending vein is ligated and the common pulmonary vein is anastomosed to the posterior left atrium. We have found the right side approach to be technically easiest and have used it in all but three infants.[11,36] The left atrium is opened from the interatrial septum to the base of the left atrial appendage. This provides excellent exposure of the common pulmonary vein posteriorly without requiring elevation of the ventricles out of pericardium, a maneuver that may produce myocardial damage. The common pulmonary vein is then opened, and anastomosis to the posterior left atrium is carried out. The foramen ovale is closed and the communicating vein is ligated.

Truncus Arteriosus

Most patients with this lesion develp severe CHF in early infancy. Operative intervention can be palliative (PAB) or corrective (Fig. 7). Banding either of the main pulmonary artery or of its branches is associated with a high mortality rate. In our group of nine patients who

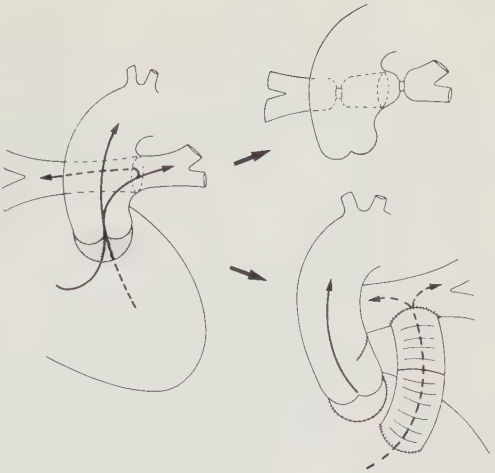

Figure 7. Truncus arteriosus in infants can be treated by banding of the main or branch pulmonary arteries, a procedure that is not often successful. Correction may be achieved by detaching the pulmonary artery from the aorta, closing the ventricular septal defect, and interposing a valve-containing conduit between the right ventricle and the pulmonary artery.

have undergone banding, only one remains a potential candidate for corrective operation. Others have had similar results.[3]

The corrective operation for truncus described by the Mayo Clinic group works well in older children who have had successful banding or have protective pulmonary stenosis.[27] In young infants, however, physiologic and technical problems relating to pulmonary artery hypertension and the small size of the patient make operation more hazardous. Furthermore, such operations are not curative at this age, since a later procedure will almost certainly be required for replacement of any conduit used in a small infant. We have attempted correction in three infants and have had no survivors, but others have reported successful cases.[13] Because of the poor results of banding, we believe that attempts at corrective operation in infancy should be made until more data can be acquired regarding mortality.

The technique of correction is removal of the pulmonary artery from the aorta followed by closure of the aorta. The right ventricle is opened and the VSD closed with a Dacron patch. A small homograft conduit is placed between the right ventricular free wall and the pulmonary artery. In older infants and children, a gluteraldehyde-fixed porcine valve conduit (Hancock) can be used.

CEREBRAL COMPLICATIONS OF HYPOTHERMIC ARREST

The organ most likely to be injured by periods of circulatory arrest is the brain. Many studies have shown that hypothermia effectively prolongs the time that circulatory arrest can be present without producing brain damage. At 20° C, the safe arrest period is over 60 minutes. In our series, 8 per cent of the infants who underwent hypothermic circulatory arrest developed seizures at some time during the postoperative period.

In these patients, the duration of circulatory arrest was not related to seizures since arrest time ranged from 18 minutes to 50 minutes. Longer periods of circulatory arrest up to 85 minutes were not associated with seizures. When they did appear, they were always transient and easily controlled with medication. No patient had electroencephalographic abnormalities prior to discharge from the hospital. Furthermore, we have seen no permanent neurologic damage.[35]

The long-term effects of hypothermic circulatory arrest on intellectual function are not yet completely worked out, but the Seattle Group has provided some late follow-up on their infants, some of whom were operated on as early as 1965.[37] Extensive psychological testing up to 7 years after hypothermic arrest demonstrated normal intellectual development in all but a few patients. Most of the few who were below the range of normal had severe postoperative problems, including cardiac arrest and renal failure. The early results of long-term follow-up therefore seem to confirm the safety of deep hypothermic circulatory arrest.

LESIONS REQUIRING PALLIATION

Some congenital heart defects cannot be corrected, or at least cannot be corrected in infancy. Such lesions can be divided into those with decreased pulmonary blood flow and those with increased pulmonary blood flow.

Those with decreased pulmonary blood flow include tricuspid atresia types A (pulmonary atresia) and B (pulmonary stenosis), single ventricle with pulmonary atresia, and TOF with an anomalous anterior descending coronary artery. These can be treated with a variety of systemic-to-pulmonary arterial shunts. Aortopulmonary shunts have the disadvantages cited above; the most serious is the possibility of too high a blood flow, resulting in CHF or late PVOD. This development may pre-

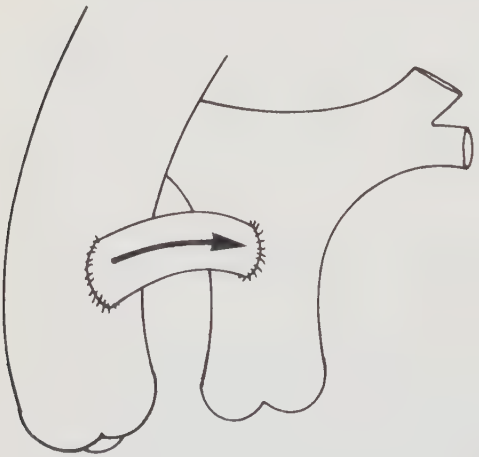

Figure 8. We have used a 4 mm prosthesis of microporous expanded polytetrafluoroethylene to construct an aortopulmonary shunt as an alternative to Blalock-Taussig anastomosis in infants.

clude corrective operation for such lesions as tricuspid atresia which require a very low pulmonary vascular resistance to be successful.

CHF and PVOD are seen far less often after Blalock-Taussig than after aortopulmonary shunts. The mortality rate after Blalock-Taussig shunts has previously been high in infants under the age of 3 months. Nevertheless, recent developments in microsurgical techniques and optical magnification have led us to reconsider the subclavian-to-pulmonary artery anastomosis for neonates requiring a shunt. Our experience is not large enough yet to evaluate the usefulness of this procedure, but we would now use either a Blalock-Taussig anastomosis or an ascending aorta-to-main pulmonary artery graft using a microporous expanded polytetrafluoroethylene prosthesis (IMPRA) in neonates who require a palliative shunt (Fig. 8). Because of the well-documented deterioration of the function of Glenn anastomoses after 5 to 8 years, we do not use these shunts in infants.

Congenital heart defects associated with increased pulmonary blood flow that cannot be corrected in infancy include tricuspid atresia type C (no pulmonary stenosis) and single ventricle without pulmonary stenosis. These are adequately treated with PAB. We tighten the band enough to make the systemic blood pressure acutely rise by 10 mm Hg and aim for a pulmonary artery pressure that is about one-half the systemic level. A systemic arterial saturation of 80 to 85 per cent is quite adequate for these patients.

REFERENCES

1. Barratt-Boyes, B. G., Simpson, M., and Neutze, J. J.: Intracardiac surgery in neonates and infants using deep hypothermia with surface cooling and limited cardiopulmonary bypass. Circulation, *43*(Suppl I):25, 1971.
2. Barratt-Boyes, B. G., and Neutze, J. M.: Primary repair of tetralogy of Fallot in infancy using profound hypothermia with circulatory arrest and limited cardiopulmonary bypass; a comparison with conventional two-stage management. Ann. Surg., *178*:406, 1973.
3. Behrendt, D. M., Kirsh, M. M., Stern, A., Sigmann, J., Perry, B., and Sloan, H.: The surgical therapy for pulmonary artery-right ventricular discontinuity. Ann. Thorac. Surg., *18*:122, 1974.
4. von Bernuth, G., Ritter, D. G., Frye, R. L., Weidman, W. H., David, G. D., and McGoon, D. C.: Evaluation of patients with tetralogy of Fallot and Potts anastomosis. Am. J. Cardiol., *27*:259, 1971.
5. Bigelow, W. G., Lindsay, W. K., Harrison, R. E., Gordon, R. A., and Greenwood, W. F.: Oxygen transport and utilization in dogs at low body temperatures. Am. J. Physiol., *160*:125, 1950.
6. Blalock, A., and Taussig, H. B.: The surgical treatment of malformation of the heart in which there is pulmonary stenosis or pulmonary atresia. J.A.M.A., *128*:189, 1945.
7. Blanco, C. E., Siassi, B., and Cabal, L. A.: Persistent patency of ductus arteriosus in premature newborn infants. Am. J. Cardiol., *31*:121, 1973.
8. Castaneda, A. R., Lamberti, J. L., Sade, R. M., Williams, R. G., and Nadas, A. S.: Open-heart surgery during the first three months of life. J. Thor. Cardiovasc. Surg., *68*:719, 1974.
9. Edmunds, L. H., Gregory, G. A., Heymann, M. A., Kitterman, J. A., Rudolph, A. M., and Tooley, W. H.: Surgical closure of the ductus arteriosus in premature infants. Circulation, *48*:856, 1973.
10. Gay, W. A., Jr., and Ebert, P. A.: Aorta-to-right-pulmonary-artery anastomosis causing obstruction of the right pulmonary artery: management during correction of tetralogy of Fallot. Ann. Thorac. Surg., *16*:402, 1973.
11. Gersony, W. M., Bowman, F. O., Jr., Steeg, C. N., Hayes, C. J., Jesse, M. J., and Malm, J.

R.: Management of total anomalous pulmonary venous drainage in early infancy. Circulation, *43,44*(Suppl. I):19, 1971.
12. Gibbon, J. H.: Application of a mechanical heart and lung apparatus to cardiac surgery. Minn. Med., *37*:171, 1954.
13. Girinath, M. R.: Case presentation: Truncus Arteriosus: Repair with homograft reconstruction in infancy. *In* Barratt-Boyes, B. G., Neutze, J. M., and Harris, E. A. (eds.): Heart Disease in Infancy; Diagnosis and Surgical Treatment. Edinburgh, Churchill & Livingston, Ltd., 1973, p. 234.
14. Girod, D. A., Hurwitz, R. A., King, H., and Jolly, W.: Recent results of two-stage surgical treatment of large ventricular septal defect. Circulation, *50*(Suppl. II):9, 1974.
15. Glenn, W. W. L.: Circulatory bypass of the right side of the heart. II. Shunt between superior vena cava and distal right pulmonary artery—Report of a clinical application. N Eng. J. Med., *259*:117, 1958.
16. Griepp, E., French, J. W., Shumway, N. E., and Baum, D.: Is pulmonary artery banding for ventricular septal defect obsolete? Circulation, *50*(Suppl II):11–14, 1974.
17. Gross, R. A., and Hubbard, J. P.: Surgical ligation of patent ductus arteriosus. J.A.M.A., *112*:729, 1939.
18. Hermann, V. M., Laks, H., Kaiser, G. G., Barner, H. B., and Willman, V. L.: The Blalock-Hanlon operation as a primary procedure for simple transposition of great vessels. Arch. Surg., in press.
19. Hikasa Y., Shirotani, H., Satomura, K., et al.: Open heart surgery in infants with an aid of hypothermic anesthesia. Arch. Jap. Chir., *36*:495, 1967.
20. Horiuchi, T., Koyamada, K., Matano, I., and Mohri, H.: Radical operation for ventricular septal defect in infancy. J. Thor. Cardiovasc. Surg., *46*:180, 1963.
21. Horsley, B. L., Carberg, D. B., Allen, A. C., Zuberbuhler, J. R., and Bahnson, H. T.: Respiratory distress from patent ductus arteriosus in the premature newborn. Ann. Surg., *177*:806, 1973.
22. Hunt, C. E., Formanek, G., Levine, M. A., Castaneda, A., and Moller, J. H.: Banding of the pulmonary artery: results in ill children. Circulation, *43*:395, 1971.
23. Kilman, J. W., Williams, T. E., Jr., Kakos, G. S., Craenen, J., and Hosier, D. M.: Intrapericardial aorta-pulmonary anastomosis for palliation of congenital heart disease. Am. J. Cardiol., *35*:149, 1975.
24. Lewis, F. J., and Tauffic, M.: Closure of atrial septal defects with the aid of hypothermia: experimental accomplishments and the report of one successful case. Surgery, *33*:52, 1953.
25. Lillehei, C. W., Cohen, M., Warden, H. E., Read, R. C., Aust, J. B., DelVall, R. A., and Varco, R. L.: Direct vision intracardiac surgical correction of the tetralogy of Fallot, pentalogy of Fallot, and pulmonary atresia defects, report of the first 10 cases. Ann. Surg., *142*:418, 1955.
26. Linde, L. M., Rasof, B., and Dunn, O. J.: Longitudinal studies of intellectual and behavioral development in children with congenital heart disease. Acta. Paediat. Scand., *59*:169, 1970.
27. McGoon, D. C., Rastelli, G. C., and Ongley, P. A.: An operation for the correction of truncus arteriosus. J.A.M.A., *205*:69, 1968.
28. Mohri, H., Hessel, E. A., II, Nelson, R. J., Matano, I., Anderson, H. N., Dillard, D. H., and Merendino, K. A.: The use of rheomacrodex and controlled hyperventilation in prolonged circulatory arrest under deep hypothermia induced by surface cooling; a method for open heart surgery in infants. Am. J. Surg., *112*:241, 1966.
29. Muller, W. H., Jr., and Dammann, J. F., Jr.: Treatment of certain congenital malformations of the heart by the creation of pulmonary stenosis to reduce pulmonary hypertension and excessive pulmonary blood flow. Surg. Gynec. Obstet., *95*:213, 1952.
30. Murphy, D. A., Outerbridge, E., Stern, L., Karn, G. M., Jegier, W., and Rosales, J.: Management of premature infants with patent ductus arteriosus. J. Thorac. Cardiovasc. Surg., *67*:221, 1974.
31. Potts, W. J., Smith, S., and Gibson, S.: Anastomosis of the aorta to the pulmonary artery. J.A.M.A., *132*:627, 1946.
32. Reul, G. J., Kabbani, S. S., Sandiford, F. M., Wukasch, D. C., and Cooley, D. A.: Repair of coarctation of the thoracic aorta by patch graft aortoplasty. J. Thorac. Cardiovasc. Surg., *68*:696, 1974.
33. Rush, B. F., Wilder, R. J., Fishbein, R., and Ravitch, M. M.: Effects of total circulatory standstill in profound hypothermia. Surgery, *50*:40, 1961.
34. Sade, R. M., Sloss, L., Treves, S., Bernhard, W. F., and Castaneda, A. R.: Correction of tetralogy of Fallot after aorto-pulmonary anastomosis. Circulation, *50*(Suppl. III):72, 1974.
35. Sade, R. M., Williams, R. G., and Castaneda, A. R.: Corrective surgery for congenital cardiovascular defects in early infancy. Am. Heart J., in press.

36. Shumacker, H. B., Jr., and King, H.:A modified procedure for complete repair of total anomalous pulmonary venous drainage. Surg. Gynec. Obstet., *112*:763, 1961.
37. Stevenson, J. G., Stone, E. F., Dillard, D. H., and Morgan, B. C.: Intellectual development of children subjected to prolonged circulatory arrest during hypothermic open heart surgery in infancy. Circulation, 50(Suppl. II):54, 1974.
38. Tay, D. J., Engle, M. A., Ehlers, K. H., and Levin, A. R.: Early results and late developments of the Waterston anastomosis. Circulation, 50:220, 1974.
39. Van Praagh, R. V., Harken, A. H., Delisle, G., Ando, M., and Gross, R. E.: Total anomalous pulmonary venous drainage to the coronary sinus. J. Thorac. Cardiovasc. Surg., *64*:132, 1972.
40. Venugopal, P., Olszowka, J., Wagner, H., Vlad, P., Lambert, E., and Subramamian, S.: Early correction of congenital heart disease with surface-induced deep hypothermia and circulatory arrest. J. Thorac. Cardiovasc. Surg., 66:375, 1973.
41. Waterston, D. J.: The treatment of Fallot's tetralogy in infants under the age of one year. (in Czech) Rozhl. Chir., *41*:183, 1962.
42. Zachman, R. D., Steinmetz, G. P., Botham, R. J., Graven, S. N., and Ledbetter, M. K.: Incidence and treatment of the patent ductus arteriosus in the ill premature neonate. Am. Heart J., 87:697, 1974.

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Transplantation in Children

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The vascularized organs most often transplanted in children are the kidney and liver. A small number of infants or children with untreatable congenital heart lesions who die early in life could possibly benefit from heart transplants, but there has been little experience with heart replacement in the pediatric age group. An occasional infant with a short bowel syndrome resulting from a complication of a congenital intestinal malformation might benefit from small bowel transplantation, but experimental bowel transplants in the laboratory have been so unsuccessful that this approach has rarely been attempted in pediatric patients. Bone marrow transplants are done in most centers by pediatric hematologists rather than by surgeons, and that form of transplantation will not be considered in this report.

The following analysis of kidney and liver transplantation in children will focus on the experience at the University of Colorado Medical Center. The pediatric kidney transplantation cases previously reported in 1966[*] and 1971[3] will be updated, with a minimum postoperative follow-up of 6 years. The comments on liver transplantation will be

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based upon 56 consecutive recipients of orthotopic livers who were 18 years of age or younger at the time of operation and who have a potential follow-up of at least 1 year.

KIDNEY TRANSPLANTATION

Kidney transplantation was performed in 57 children 3 to 18 years of age between November, 1962 and July, 1969. Twenty-two of these patients were operated upon 10 to 13 years ago and the other 35 cases 6 to 10 years ago.

Conditions of Care

The methods of transplantation and immunosuppression have been described previously.[3, 4, 6, 8-11] Fifty-five of the children had hemodialysis before transplantation, and 18 had peritoneal dialysis. Almost all of the children had bilateral nephrectomy and splenectomy, either before or at the same time as transplantation. Thymectomy was done in 10 patients. The 22 children treated with renal transplantation between 1962–1965 were given their primary kidneys by living donors. There were 20 living related donors and two living unrelated donors. In the 35 cases transplanted between 1965 and 1969, 25 of the primary homografts were

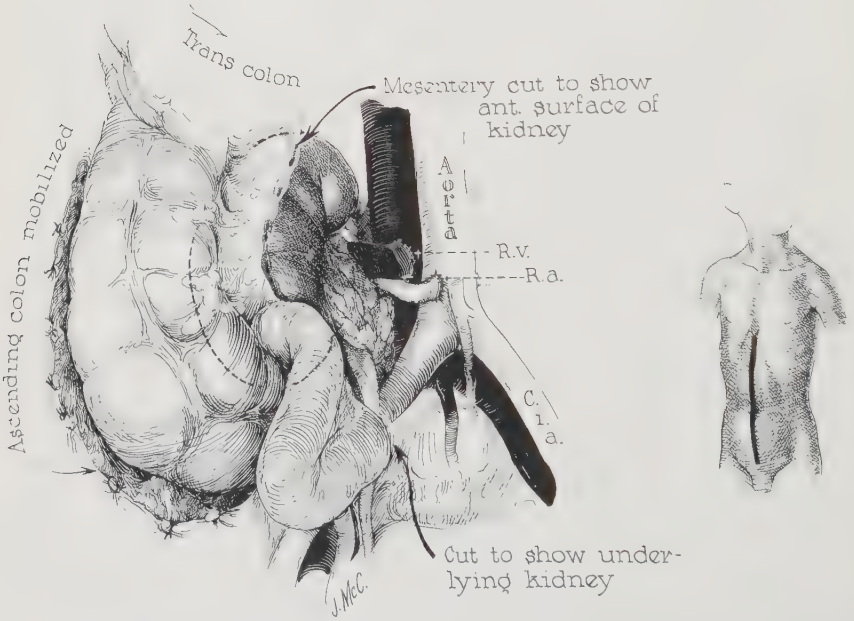

Figure 1. Technique used for transplantation of adult homografts to infants or small children. The entire operation is performed transabdominally, through a midline incision. (Reproduced from Starzl, T. E., Marchioro, T. L., Morgan, W. W., and Waddell, W. R.: A technique for use of adult renal homografts in children. Surg. Gynec. Obstet., *119*:106, 1964. By permission of Surgery, Gynecology & Obstetrics.)

Figure 2. A 25-year-old laboratory technician who was the first recipient of a renal homograft in the Denver series, in 1962, at age 12 years; retransplantation was necessary in 1968. Renal function is normal.

from living related donors and the other 10 first organs were from cadavers. In 11 children the graft was put retrocecally via a transperitoneal approach, because of the small size of these recipients (Fig. 1). The bladder was usable for restoration of urinary tract continuity in all cases. Sixteen of these 57 children have subsequently required retransplantation.

Donor selection by means of histocompatibility testing was started in Denver in October, 1964, and between then and 1966, all donors were chosen by HLA matching. This method of donor selection was discontinued in 1966 because of the lack of correlation between the HLA match and graft survival. Typing was continued thereafter in all cases for the sake of data accumulation. Because of the age of the recipients there were few sibling donors. For example, only one sibling donor was used for the 22 patients transplanted between 1962 and 1965. The most common donors were parents.

Grafts obtained from living donors were perfused immediately after removal with cold lactated Ringer's solution (15°) which contained 50 mg heparin and 1 gm procaine per liter. Grafts obtained from cadaveric donors were preserved in a variety of ways, all of which included prompt cooling with chilled solutions.

All 57 children received prednisone and azathioprine. The last 28 cases received antilymphocytic globulin (ALG) as well, usually for a period of less than 4 months after transplantation. A few of the earliest patients received actinomycin C and local graft irradiation for acute rejection crises. The first patient in the series who received a homograft, in November, 1962, at the age of 12 years, was subjected to total body irradiation (Fig. 2).

The native kidney disease causing renal failure was not clearly identifiable in all cases. Of the 22 patients transplanted between 1962 and 1965, the original disease was chronic glomerulonephritis in 18 cases, pyelonephritis in three, and polycystic disease in one. Similarly, most of the 35 children transplanted between 1965 and 1969 had chronic glomerulonephritis; there was one case of cystinosis and one case of oxalosis.

Outcome

Five primary kidneys were lost in the early postoperative period. One graft which was transplanted from an A donor into an O pediatric recipient early in our experience failed immediately from hyperacute rejection. Three grafts were rejected hyperacutely due to presumed or proved preformed antibodies against non-red cell antigens. A fifth graft was removed 3 days after transplantation because of a technical complication.

After follow-ups of 6 to 13 years, 35 (61 per cent) of the 57 children are still living and 34 (60 per cent) have renal function. One is on dialysis (Table 1).

Fourteen (64 per cent) of the 22 children originally treated 10 to 13 years ago are alive, five after undergoing retransplantation.

Twenty-one (60 per cent) of the 35 patients transplanted 6 to 10 years ago are alive. Fifteen (60 per cent) of the 25 children whose primary grafts were from related volunteers are still alive, as well as six (60 per cent) of the ten children whose primary grafts were from cadavers. Of the 21 current survivors from the 35 cases of 6 to 10 years ago, 16 still have the original grafts and five bear retransplants.

The greatest mortality was within the first few months postoperatively, although losses occurred as late as 12 years. The leading cause of death was infection. There were two deaths from cerebrovascular accidents. One patient died from a pulmonary embolus.

Unusual causes of death included reticulum cell sarcoma of the brain in a 14-year-old child who died 7 months after transplantation from a relative. One child received her first renal homograft in 1968, her second in 1970, and died in 1973 at the age of 18 years of superior mesenteric arterial occlusion. One 18-year-old boy committed suicide 8 months after successful related transplantation, by jumping through a heavy glass window on the 8th floor of the hospital.

The leading cause of graft failure was rejection. Technical difficulties were rare, accounting for one lost graft in the earlier 22 cases. Three patients are known to have stopped taking immunosuppressive medication, against medical advice. They were 18 to 22 years old when they discontinued medication, and all three lost their grafts to rejection within 6 months after discontinuing azathioprine and prednisone. These grafts had previously been functioning well for 3 years, 6 years, and 7 years respectively. All three patients were successfully retransplanted, but one died 17 months later of hepatitis and bacterial sepsis.

Table 1. *Results of Pediatric Kidney Transplantation in 57 Children*

NO. OF CASES	DURATION OF FOLLOW-UP	DONOR		NO. LIVING
		Living	Cadaver	
22	10 to 13 years	22*	0	14† (64 per cent)
35	6 to 10 years	25	10	21‡ (60 per cent)

*Two living unrelated donors. All other donors were related.
†Five living after retransplantation.
‡Five living after retransplantation.

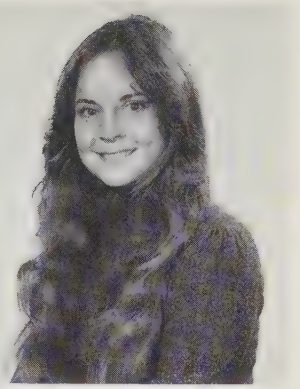

Figure 3. Twelve years ago this young lady received a renal homograft from her mother, at age 10 years. She is currently enrolled in our university's Child Health Associate Program.

Twelve of the 57 children had one retransplant, one has had three transplants, one has had four transplants, and two have had five transplants. One child with five transplants is alive with a functioning graft 13 years after the original transplantation. The other recipient of five transplants died 3 months after the 5th transplant. Six of the 16 children who underwent retransplantation have died.

Most of these patients have had some "catchup" growth following transplantation, as we have previously reported,[3] although most have ended up with short stature. A few children have experienced bony complications in addition to growth retardation, including atrophy of the femoral head in five patients and compression fractures of lower thoracic vertebrae in one patient.

In spite of the additional burdens imposed on these children by end-stage renal failure, hemodialysis, transplantation, and immunosuppression, many of the 35 surviving patients have been able to develop into well-adjusted young adults. All of the 22 survivors, whose current ages range from 14 to 30 years, are now working full-time or are going to school full-time or are raising families. One 22-year-old girl, who received a transplant 12 years ago from her mother and is in excellent health, recently married a transplant surgeon (Fig. 3).

LIVER TRANSPLANTATION

During the 11-year period 1963 to 1974 approximately 200 patients received liver replacement. Almost 100 of these recipients were from the Denver series, including 56 who were 18 years old or younger at the time of transplantation. The diseased native liver was removed and the cadaveric organ was placed in the normal (orthotopic) anatomic location (Fig. 4). These 56 children are the subject of the following report.

Case Material

In 40 of the children the cause of liver failure was biliary atresia. The other diagnoses were hepatitis (nine cases), malignant tumor (three

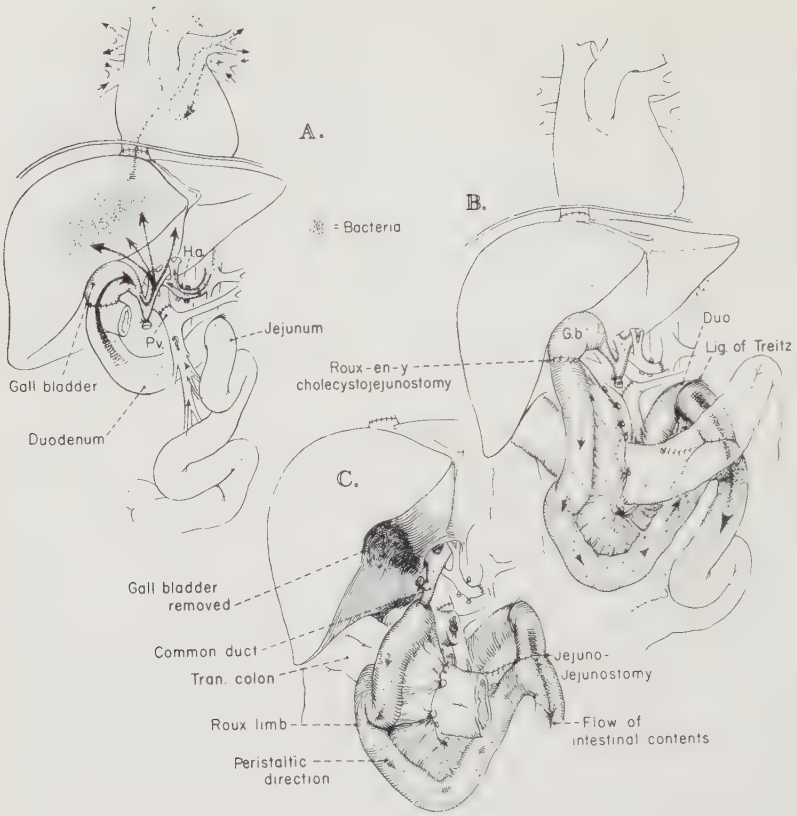

Figure 4. Technique of orthotopic liver transplantation. In pediatric patients, three different kinds of biliary reconstruction have been employed: *A*, Cholecystoduodenostomy: this simple technique carries the greatest risk of bacterial contamination of the biliary tract. *B*, Roux-en-Y cholecystojejunostomy: the biliary tract of the homograft is separated from the main gastrointestinal stream by an 18-inch isoperistaltic limb of jejunum. *C*, Roux-en-Y choledochojejunostomy: the duct-to-bowel anastomosis is simple if the duct has become dilated, as is the case when conversion from (*B*) to (*C*) is necessary. (Reproduced from Starzl, T. E., Ishikawa, M., Putnam, C. W., et al.: Progress in and deterrents to orthotopic liver transplantation; with special reference to survival, resistance to hyperacute rejection, and biliary tract reconstruction. Transplant. Proc., 6 (Suppl. 1):129, 1974. Used with permission.)

cases), Wilson's disease (two cases), alpha-1-antitrypsin deficiency (one case) , and congenital biliary cirrhosis (one case).

At the time of transplantation the mean age of the 40 patients with biliary atresia was 42.0 ± 37.7 (S.D.) months, with an age range of 3 to 191 months. Four of these children had survived 7 to 15 years before transplantation and were thought to have intrahepatic atresia because of their longevity. Under the light microscope the livers of these four children showed micronodular biliary cirrhosis, compatible with congenital intrahepatic biliary atresia. Two of these four livers were found to contain hepatoma, which was found in only one of the 36 younger children transplanted for biliary atresia.

The mean age of the 16 children transplanted for diseases other than biliary atresia was 12.9 ± 4.6 (S.D.) years, with an age range of 1 to 18 years.

Conditions of Care

Very young cadaver organ donors are scarce, largely because lethal head trauma is less common in the young child than in the teenager or adult. At the same time, it is important that the donor liver be small enough to fit easily into the peritoneal cavity of the recipient. An oversized organ is difficult to revascularize, because of the relatively fixed distance betwen the suprahepatic vena cava and infrahepatic vena cava in the recipient. In addition, an excessively large graft may cause postoperative respiratory insufficiency by restricting diaphragmatic motion.

The size of the donor (liver) is the major criterion for donor selection. Preformed antibodies in the recipient against the donor's A or B red cell antigens or against the donor's HLA antigens do not seem to have so ominous a prognosis in liver transplantation as in kidney transplantation. Neither of the two children who had liver transplants in the face of preformed anti-red cell antibodies had hyperacute rejection of the graft, such as was described in the section on renal transplantation. However, neither of these children survived for longer than 8 months after transplantation.

The technique of operation has been described.[2, 5, 12] For the last 2 years, including the last year of this report (1974), biliary drainage of the graft has been established by anastomosis of the gallbladder to the jejunum (Roux-en-y) (Fig. 4*B*), rather than by cholecystoduodenostomy (Fig. 4*A*). Choledochojejunostomy (Fig. 4*C*) or choledochocholedochostomy with T-tube splint have been used in a few cases.

Splenectomy was done in 42 of the first 56 pediatric cases and during that period was omitted only if this procedure appeared to add excessive risk to the transplant operation; in the last five children included in this report, it was decided preoperatively that splenectomy would not be done.

Immunosuppression for these patients has been described.[5, 7, 12] Prednisone, azathioprine, and antilymphocytic globulin were used, and intravenous methylprednisolone was given intermittently for acute rejection episodes.

Outcome

Biliary Atresia. Twenty-nine of the 40 patients with biliary atresia died within 6 months of transplantation. Ten patients died within the first 3 postoperative weeks because of vascular occlusions or hemorrhage. Two of these 10 deaths occurred following retransplantation; in one patient the original graft appeared to have been destroyed by viral infection, and in the other patient the original graft from an anencephalic monster appeared to have previously unrecognized intrahepatic biliary atresia.

Five additional early postoperative deaths, within the first 5 post-

operative weeks, were thought to be due to rejection. These patients were treated with heavy immunosuppression, and infections were important contributory factors in the deaths of almost all of these patients. At autopsy the histology of four of these grafts showed mononuclear cells in the portal tracts and around the central veins, with necrosis of hepatocytes, compatible with acute cellular rejection. The histology of the fifth liver was not characteristic of rejection; therefore, this clinical diagnosis could not be confirmed.

Seven patients died 1 to 3 months after transplantation because of nonvascular technical complications. One patient died of a fungal retroperitoneal abscess following injury to the tail of the pancreas during splenectomy. The other six deaths followed complications related to the biliary tract reconstruction. Four patients with cholecystoduodenostomy developed cystic duct obstruction, and two more had biliary fistulas. At autopsy these six livers showed microscopic evidence of partial biliary obstruction. There was no histologic evidence of rejection.

There were seven deaths 2 to 6 months after transplantation because of infection. Four of these seven deaths were related to partial hepatic infarctions which were thought to be due to occlusion of small branches of the hepatic artery; these areas of infarction became infected. The infectious agents varied in the seven cases and included bacteria, fungi, and viruses.

The 11 patients who survived for more than 6 months after transplantation all survived for at least 6 additional months. Four subsequently died 1 to 3½ years after transplantation because of liver damage of uncertain cause. Chronic rejection was probably a major factor in all four of these deaths; hemophilus influenza septicemia and viral hepatitis may have been contributory in two cases. The other seven patients are still alive 1 to 5 years after transplantation (Fig. 5).

OTHER THAN BILIARY ATRESIA. Seven of the 16 patients died within 6 months of operation. One succumbed in 10 postoperative days with liver necrosis, probably related to hepatic arterial occlusion, although it is possible that this liver was damaged in the donor or while being transferred to the recipient. One patient developed irreversible early rejection of the graft requiring transplantation on the 157th postoperative day; she died 1 month later of sepsis. There was one additional early death from acute cellular rejection, on the 9th postoperative day. One patient died on the 64th postoperative day from sepsis following perforation of a diverticulum of the right colon. There were two additional deaths from nonvascular intraabdominal complications; both patients had partial biliary obstructions and died of sepsis. One patient died of carcinomatosis 143 days after resection of a hepatoma.

Nine (56 per cent) of the 16 children survived for at least 1 year after transplantation. Two children with hepatoma died 13 and 14 months after transplantation, of carcinomatosis. One child died 26 months after transplantation with obstruction at the choledochocholechostomy; in this patient inability to enter dilated biliary radicals during percutaneous transhepatic cholangiography was incorrectly interpreted as assurance against the presence of biliary obstruction. One teenager died 6 years after liver replacement for Wilson's disease. This transplant

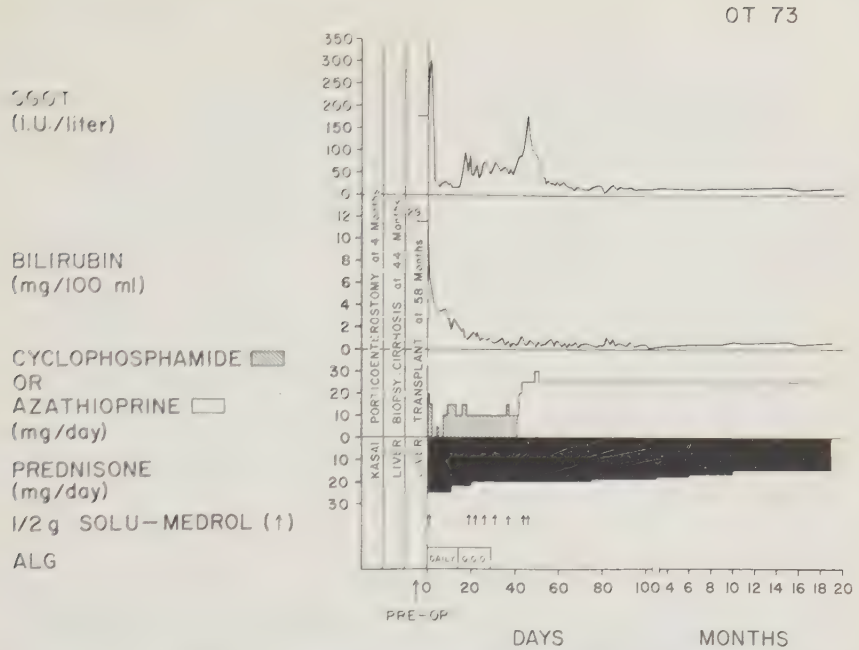

Figure 5. The course of a child with biliary atresia in whom the porticoenterostomy of Kasai had failed to relieve her jaundice. She is now alive 2 years after hepatic transplantation and has completely normal liver function. (By permission of Josiah Macy, Jr. Foundation.)

had completely corrected the serum copper and ceruloplasmin levels and had partially normalized the urine copper excretion. The cause of death was chronic rejection and partial biliary obstruction.

Five of the 16 patients transplanted for diseases other than biliary atresia are still alive 1 to 4½ years after transplantation. Their primary diseases were chronic aggressive hepatitis (three), Wilson's disease (one), congenital biliary cirrhosis (one), and alpha-1-antitrypsin deficiency (one).

The results of liver replacement in these children in which potential follow-up is at least 1 year after transplantation are summarized in Table 2.

Table 2. *Fifty-Six Pediatric Liver Transplants: Mortality During the First Year After Transplantation*

	BILIARY ATRESIA (40)	NONBILIARY ATRESIA (16)
Deaths from vascular complications	10	1
Deaths from early rejection	5	2
Deaths from nonvascular intraabdominal complications	7	3
Deaths from infection	7	0
Deaths from recurrent cancer	0	1
1 year survival	11/40 (28 per cent)	9/16 (56 per cent)

CONCLUSIONS

Kidney transplantation in very young children, less than 2 years of age, has usually failed, mainly because of difficulties maintaining these patients on hemodialysis long enough to permit retransplantation after loss of the original graft.[1] Liver replacement in the very young child has been associated with a higher frequency of vascular and biliary obstruction than in the older child, due to the small size of these structures. Such accidents have contributed to unsatisfactory results with biliary atresia.

Transplantation of kidney or liver into older children has been more successful than transplantation of these organs into adults. Related or cadaveric kidney transplantation in the child has been followed by at least a 60 per cent patient survival for 6 to 13 years and a very acceptable quality of life. Liver replacement for diseases other than biliary atresia has been followed by a 56 per cent 1-year survival rate, and two children have survived for more than 5 years.

REFERENCES

1. DeShazo, C. V., Simmons, R. L., Bernstein, D. M., DeShazo, M. M., Willmert, J., Kjellstrand, C. M.,and Najarian, J. S.: Results of renal transplantation in 100 children. Surgery, 76:461, 1974.
2. Lilly, J. R., and Starzl, T. E.: Liver transplantation in children with biliary atresia and vascular anomalies. J. Ped. Surg., 9:707, 1974.
3. Lilly, J. R., Giles, G., Hurwitz, R., et al.: Renal homotransplantation in pediatric patients. Pediatrics, 47:548, 1971.
4. Starzl, T. E.: Experience in Renal Transplantation. Philadelphia, W. B. Saunders Co., 1964.
5. Starzl, T. E., and Putnam, C. W.: Experience in Hepatic Transplantation. Philadelphia, W. B. Saunders Co., 1969.
6. Starzl, T. E., Marchioro, T. L., Morgan, W. W., and Waddell, W. R.: A technique for use of adult renal homografts in children. Surg. Gynec. Obstet., *119*:106, 1964.
7. Starzl, T. E., Ishikawa, M., Putnam, C. W. et al.: Progress in and deterrents to orthotopic liver transplantation; with special reference to survival, resistance to hyperacute rejection, and biliary tract reconstruction. Transplant. Proc., 6(Suppl. 1):129, 1974.
8. Starzl, T. E., Marchioro, T. L., Porter, K. A., et al.: The role of organ transplantation in pediatrics. PED. CLIN. N. AM., *13*:381, 1966.
9. Starzl, T. E., Porter, K. A., Halgrimson, C. G., et al.: A decade follow-up in early cases of renal homotransplantation. Ann. Surg., *180*:606, 1974.
10. Starzl, T. E., Porter, K. A., Husberg, B. S., et al.: Renal homotransplantation. Part I. Curr. Probl. Surg., April, 1974.
11. Starzl, T. E., Porter, K. A., Husberg, B. S., et al.: Renal homotransplantation, Part II. Curr. Probl. Surg., May, 1974.
12. Starzl, T. E., Porter, K. A., Putnam, C. W., et al.: Liver Replacement in Children. Proceedings of the Josiah Macy, Jr. Foundation, Paris, 1975 (in press).

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Primary Excision and Prompt Grafting as Routine Therapy for the Treatment of Thermal Burns in Children

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Burn therapy, although remarkably improved, remains a long, complicated process, and the patient remains at serious risk for weeks or months. The development of methods of topical burn treatment through the use of such agents as silver nitrate,[13] Sulfamylon,[12] and silver sulfadiazine[1] has provided a high degree of protection against burn wound sepsis. These developments, in turn, have resulted in improved burn care and decreased overall mortality. This decrease, however, has been most marked in patients with injuries ranging from 10 to 40 per cent of the body surface area. For patients with massive burns the mortality rate, until recently, has continued close to 100 per cent. At the same time, improved understanding of the burn injury and its pathophysiologic complications has served to emphasize an important factor—that while mortality is clearly related to the total area of burn injury, it is more significantly related to the extent of full-thickness (third degree) destruction of the skin. Realistically, the cause of death in the severely burned child is not simply a result of the thermally destroyed skin but, more specifically, a result of the metabolic and bacterial consequences of a large open wound present for a long time. An examination of the overall treatment method involved in the use of topical agents in burn therapy indicates that, while extremely helpful in preventing burn wound sepsis, they do not reduce the long time between injury and burn

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wound closure. The prolonged length of time required for wound debridement and preparation for grafting increase the probability of invasive infection, and allow for extensive fluid, protein, and heat loss as well as for homeostatic, metabolic, and allergic side effects caused by the topical agents themselves. Further, and perhaps most important, the open, contaminated burn wound provides the stimulus for a neural-endocrine response leading to the extensive catabolic state so well recognized following burn injury. Thus, an extensive, full-thickness burn remains a lethal injury not because of the burn itself, but because it creates an extensive, open wound which, in the usual system of burn care, is not closed soon enough to prevent metabolic exhaustion and invasive infection. Therefore, a system of burn care which will be most effective calls for eschar excision and wound closure to take place before the secondary complications of burn injury (malnutrition and sepsis) take place.

The original clinical experience at Massachusetts General Hospital with primary excision and immediate grafting as the definitive treatment for thermal burns was reported in 1947.[8] The bacterial and physiologic problems following primary excision resulted in the procedure being discontinued except for well circumscribed areas of obvious full-thickness burn injury. Prompted by improved techniques of controlling sepsis and a growing knowledge of the physiologic problems, re-evaluation showed that excision and immediate grafting, combined with silver nitrate therapy, reduces morbidity and mortality. It also shortens the burn illness to between one-third and one-half of that required for a similar sized injury treated with silver nitrate therapy alone.

The following discussion provides a description of a routine method of treatment of deep dermal and/or full-thickness burn injuries based on primary excision and prompt wound closure. Primary, in this context, is used to denote that excision and prompt closure are the fundamental, unreplaceable factors in the treatment system, all other factors being adjuncts. Technical considerations, both operative and nonoperative, which are important to the treatment system, as well as a comparison of the results with those obtained using the classic 0.5 per cent silver nitrate method, are included.

In this report, burn size is designated as small (0 to 19 per cent of the body surface area [BSA]); medium (20 to 44 per cent BSA); large (45 to 75 per cent BSA); and massive (75 to 95 per cent BSA). These divisions divide patients into groups according to the techniques required for prompt wound closure, rather than into groups according to increasing mortality. For example, there are ample donor sites available in small burns. In medium-sized burns, however, donor sites must be harvested extensively; also, uncommon donor sites, such as scalp and feet, must be used to accomplish prompt wound closure. For large burns donor sites are clearly inadequate for prompt closure; this can be accomplished only by the combined use of autograft and viable cadaver allograft. (Fortunately, the time required for beginning allograft rejection is about the same as that required for donor site regeneration. Thus at about 14 days following initial allografting the patient is returned to the operating room, the allografts are removed, and the wound is permanently closed with autograft.) Large burns are therefore promptly closed

with a combination of autograft and allograft and only closed permanently with autograft. For massive burns the problem becomes more complex because the area of wound requiring allograft closure is considerably larger than the total area of autograft donor site available for reharvesting. In this case allograft cannot be completely replaced when it rejects in about 2 weeks, and the resulting open wound leads to malnutrition and sepsis. To prevent the recurrence of an open wound, we have used immunosuppression to delay allograft rejection long enough to allow repeated harvesting of donor sites to provide complete autograft closure. It is important to note that the extent of deep dermal or full-thickness injury, not total burn size, is the most important single factor in determining the method of treatment which will be best for the patient. For example, a 90 per cent superficial, second degree burn is best treated with topical chemotherapy without excision, while full-thickness injuries as small as 1 per cent are most effectively treated by excision and wound closure. The important variable to reduce to a minimum is the length of time the wound remains open following injury. In a superficial second degree burn, healing takes place spontaneously in a relatively short time, while with deep dermal or full-thickness injuries wound closure is prolonged. These divisions of the extent of deep dermal or full-thickness burn injury are useful in considering the exact method of primary excision and grafting, for as the deep burn size increases the methods are modified, even though the concept of primary excision and prompt closure remain the same throughout.

TECHNICAL CONSIDERATIONS

Selection of Patients

Children with deep burns (mixed deep dermal and full-thickness injuries involving up to 90 to 95 per cent of the body surface) can be treated most effectively with primary excision and prompt grafting. Patients with superficial second degree burns where clinical judgment assessed wound healing to be accomplished in 3 weeks or less were not treated with excision. In most cases excision was begun as soon as practical, usually in the 2nd to 5th day following burn injury, although an occasional excision was carried out as late as the 14th postburn day if the burn wound remained uncolonized. Late admission of patients to the burn service (10 days post injury or longer) were not subjected to excision and grafting as described in this article, nor were patients who had extensive wound colonization on admission, even if they were admitted within the first 10 days of burn injury. Excision was carried out in children of all ages if they fitted the above criteria. Patients with pulmonary burns and traumatic injuries accompanying thermal injuries were treated with excision unless their injuries specifically prevented it.

Timing and Extent of Excision

Clinical experience with primary excision for over a decade has allowed us to set certain guidelines for safe application of the method (Table 1). In general, excision is carried out as soon after injury as possi-

Table 1. *Description of Patients Undergoing Excisional Therapy*

No. of patients	100
Age of patients	3 months to 15 years
Average age	7 years
Time of excisional procedure postburn	12 hr to 18 days
Extent of excision at each operation	5 to 30 per cent BSA
Average size of single excision	17 per cent BSA
No. of operations required for complete excision	1 to 3 procedures
Total per cent of BSA excised in multiple excisions	30 to 52 per cent BSA

ble. For practical purposes, the surgical procedure is initiated as soon as metabolic and physiologic balance have been restored, with satisfactory vital signs, adequate urinary output, and a normal or near normal blood picture, including adequate hematocrit and serum proteins. This is often before the classic period of resuscitation is over. The time may vary from a few hours for small burns to several days for extensive burns, especially for those patients undergoing staged procedures. In general, the earlier the operative excision is carried out the better it is tolerated by the children.

The extent of body surface area excised at each operation may vary from 5 to 30 per cent, with an average of 17 per cent BSA for a single excision, in our experience.

Selection of Area to Excise

Survival is the primary consideration in the treatment of the victim of extensive thermal injury. The main objective of therapy, therefore, is to achieve maximum reduction in the size of the burn wound, so that excision and grafting should eliminate as wide an area of burn wound as possible. In large burns where more than one excision is necessary, the choice of area of first excision has proven important. It is best to excise first those anatomic areas that provide a large area, where it is easy to apply and hold the graft in place. The chest, abdomen, flank, and back are easily excised; and graft takes over these areas approach 100 per cent. Excisions on extremities (arms and legs) almost never produce a 100 per cent take, often less than 90 per cent. Because of this, in performing staged operations for extensive burns it is wise to do the trunk first, followed by excision and grafting of the extremities.

For smaller burns, where survival is not a primary concern and especially where particular anatomic areas such as the hands are involved, the goal is preservation and restoration of function. To achieve this objective in the hand, for instance, it is necessary to deal with the acute burn injury expeditiously. Early and accurate burn excision with immediate resurfacing provides the best opportunity to prevent the development of serious physical disability or crippling deformity. The same surgical technique is used for excision of burns of the hand as for excision of other cutaneous burns, as described below.

OPERATIVE MANAGEMENT OF THE PATIENT

Coagulation factors and blood volume and composition are brought to normal preoperatively and maintained during operation through solutions containing appropriate colloid, electrolyte, and cells delivered by intravenous catheters placed as centrally as possible. In extensive third degree burns the platelet count in the early postburn period may be reduced. If the platelet count drops to 60,000 or below, platelets are transfused immediately preoperatively and the platelet count kept above 60,000 during the operative period to prevent excessive bleeding. In the early postburn period where sepsis is not involved, platelet transfusions, eschar excisions, and wound closure have been successful in repairing platelet abnormalities. Persistent platelet-induced bleeding, extending into the postoperative period and requiring repeated platelet transfusions, has not been a problem.

The established techniques of tourniquets, ligation of major vessels, and electrocoagulation are employed appropriately. Tourniquets are effective in limiting initial loss from extremities, but their release is followed by a reactive hyperemia. Pressure with elastic bandages is used on donor sites and intraoperatively on excised areas of extremities. Electrocoagulation alone provides control of punctate bleeding sufficient to permit immediate grafting when sequential excision is done at the dermal level.

The operation is planned and conducted with a flexibility that allows terminating it if blood loss becomes excessive. Loss of more than one estimated blood volume is seldom exceeded. Where operative blood loss is great or difficult to control, the operation is divided into stages a day or two apart rather than incurring periods of poor tissue perfusion which favors invasive sepsis or deterioration of the coagulation factors that accompanies massive blood replacement. As the interval between burn injury and operation lengthens, the vascularity and contamination of the wounds increase and the patient's compensatory mechanisms appear to weaken. While the primary objective of immediate closure of the area excised is generally attainable, staged or limited operations are preferable to the physiologic derangements that accompany major blood loss.

Penicillin was administered for the first 5 days following the burn. Preventive antibiotics, specifically chosen on the basis of the antibiotic sensitivities of the wound flora, were given preoperatively and discontinued postoperatively for each operation. Other systemic antibiotics were given only following specific clinical and bacteriologic evidence of invasive infection.

In order to reduce blood loss, hypotensive anesthesia was used in patients whose area of excision plus the area of donor sites amounted to more than 30 per cent of the body surface area. Red blood cell replacement was carried out with the use of fresh frozen red cells and plasma replacement with fresh frozen plasma.[10]

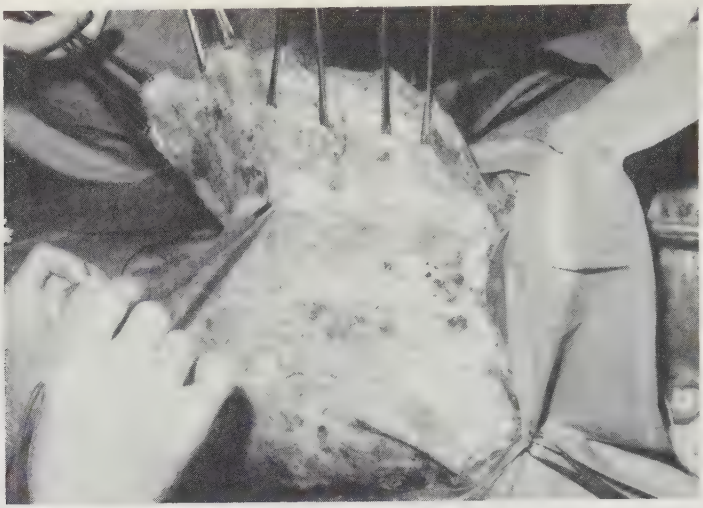

Figure 1. Fascial excision of the anterior chest wall using an electrosurgical knife.

TECHNIQUES OF PRIMARY EXCISION

In the operative treatment of burn patients, primary excision of deep dermal and/or full-thickness burns has utilized two[12] surgical techniques: the first technique, which we have called fascial excision, is the direct excision of the entire thickness of the destroyed skin and subcutaneous tissue down to the level of deep fasciae. This type of excision is reserved for large areas of well defined, unequivocal deep full-thickness injury involving an entire anatomic area, such as neck, chest, back, or extremities. In patients who are found to have deep thermal injury that extends below the fascia, debridement must be carried out to include all devitalized tissues, including muscle if involved, at the initial debridement. Excision down to the fascial level for the most part is performed using an electrosurgical knife, and hemostasis is achieved with electrocoagulation and the use of fine hemostats (Fig. 1). The use of an electrocautery knife has significantly minimized both blood loss and the time required for the operative procedure. Although electrocautery causes microscopic foci of tissue injury, this is not significant enough to interfere with the uniform success of skin graft take.[11] Because grafting of the excised wound is almost always carried out during the same operative procedure, complete hemostasis is indispensable to obtain as near a 100 per cent graft take as possible. During this procedure the edge of the wound where skin grafts join normal skin is an area which requires careful attention. Here, the step-off between normal skin and wound bed causes difficulties. Subdermal bleeding at the skin edge, both immediate and delayed, makes effective hemostasis difficult. Movement of the unburned skin edge on the subcutaneous tissue at the wound edge presents a hazard to an accurate junction and healing of skin graft and normal skin edge. In order to stabilize the wound edge, eliminate the

step-off, and obtain effective hemostasis, a continuous over-and-over 3–0 chromic suture is used to bring the leading skin edge accurately down to the fascia in a stable manner. Skin grafting is then carried to this skin edge and secured with interrupted 5–0 chromic stitches and adhesive strips.

The second technique, which we have called "sequential eschar excision,"[5] is used where the burn is a mosaic of deep dermal and full-thickness injury, without extensive involvement of the subcutaneous tissue. In this method of excision a freehand knife is used with the guide set at approximately 6/1000 inch, and the burn eschar is removed in a sequential fashion. Successive slices are removed from an area until pink dermis is encountered with multiple bleeding points. Below areas of full-thickness loss, if the subdermal or subcutaneous veins are thrombosed, several slices should be made until all thrombosed venous tissue and brown fat have been completely removed (Fig. 2). All nonviable tissue must be excised to avoid the hazard of complete loss of graft. As in fascial excision, complete and accurate hemostasis is essential before grafting is carried out. In this technique, bleeding, particularly that encountered in the papillary dermis, may be troublesome, so that excision should not be carried out to completely remove the total area of burned tissue, say of the chest or extremities, before hemostasis is begun. Rather, excision should be carried out stepwise and should be limited to a well circumscribed area of the burn, gaining hemostasis accurately in

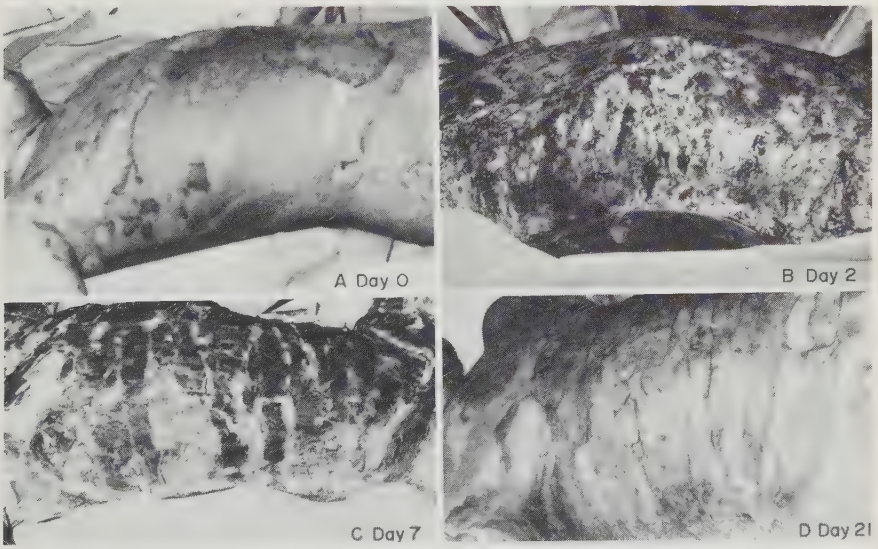

Figure 2. *A*, Well defined full-thickness burns involving anterior chest and lower abdomen on day of admission. *B*, Full-thickness burn of the chest and abdomen directly excised through the entire thickness of the burned skin and the subcutaneous tissue down to the level of deep fascia. *C*, Excised and autografted anterior trunk on day 7 (5th postoperative day), showing complete wound closure with sheet autografts taped together with Steri-Strips. The grafts as well as the patient's skin are discolored with 0.5 per cent $AgNO_3$. *D*, Three weeks after admission, the primarily excised and autografted area completely healed with minimal scarring and contracture.

this area before starting in another area. Following excision and accurate hemostasis, grafting is carried out immediately. All debrided tissue is grafted, including the dermal elements remaining following excision of a deep dermal burn. Any excised dermis left exposed and ungrafted may desiccate rapidly to form a new slough.

In certain cases, particularly in the excision of extremity burns, bleeding can be excessive and may require more than optimal blood replacement before accurate hemostasis can be achieved with electrocautery. In these cases where excessive bleeding is recognized, major vessels should be controlled with cautery but control of bleeding from the multiple minute bleeding points should be obtained with a carefully wrapped, firm dressing soaked with saline to prevent tissue injury. Auto- or allografting can then be carried out in 24 hours. However, in excision of hand burns a 24-hour delay in grafting has provided a decrease in efficiency of graft take, so that immediate grafting of hands is recommended. It is our opinion that immediate grafting of an excised wound is most likely to provide a near 100 per cent take, but only if accurate hemostasis is obtained and blood loss is held to a satisfactory level.

METHOD OF GRAFTING AND PRIMARY WOUND CLOSURE

Split-thickness skin grafts are obtained with an air driven dermatome. If grafting is to be done immediately, the graft is obtained at the same operative procedure, but usually before excision of the burn eschar. When grafting is delayed by 24 hours, grafts are not harvested at the time of excision but at the time of grafting. Autografts or allografts are applied to close the entire wound and are secured in place along the wound margins with interrupted 5–0 Dexon or chromic sutures, while the edges between each strip of graft are taped together with adhesive strips to avoid leaving gaps between each graft (Fig. 3). Occasionally it is not possible to cover completely a freshly excised burn with autograft, particularly following large excisions. Although the objective of wound repair is total primary closure with sheet graft, if the shortage of autograft will leave only a relatively small area, meshed autogenous grafts expanded 3 to 1 and covered with allograft are used to provide closure of the remainder of the excised wound. If the uncovered area is large, as would be the case in a large burn, sheet allograft is used for wound closure.

In a major burn it is clear that one must harvest all available donor sites to provide the maximum amount of autograft skin. The scalp provides a most reliable donor site, not only because it is seldom extensively burned, but also the scalp in children occupies a fairly large surface area. In addition, the scalp regenerates to the point where reharvesting is possible in the shortest length of time and allows the largest number of recroppings. The feet also provide an area of skin seldom burned and available for donor site.

Grafted areas of the neck, trunk, flanks, shoulder, axillae, and groin are treated in open fashion and fluid collections under the grafts are

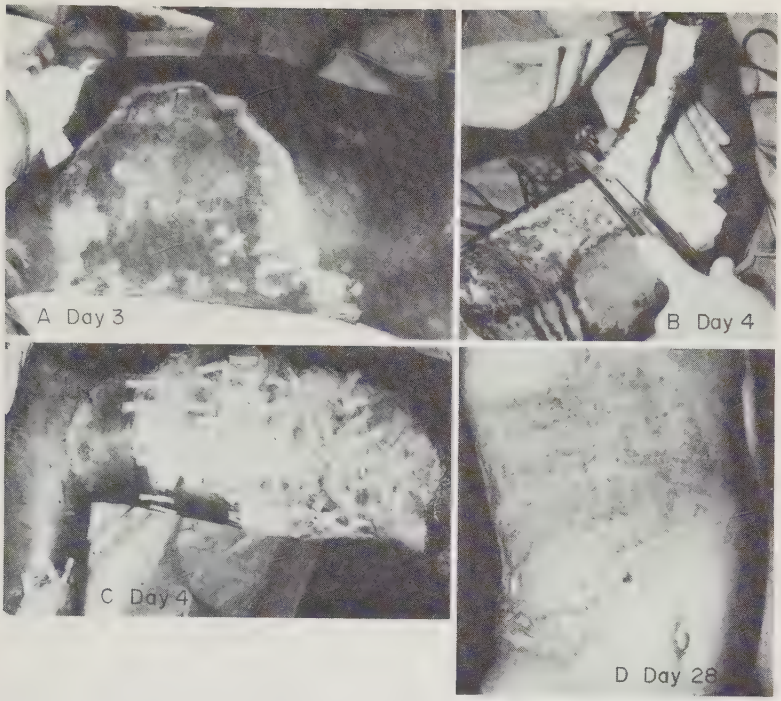

Figure 3. *A*, Flame burns involving the right chest, axilla, and right back seen on day 3. Injury was of mixed deep dermal and full-thickness injury. Black staining is caused by 0.5 per cent $AgNO_3$. *B*, Sequential eschar excision down to normal viable tissue accomplished with a free hand, guarded knife. *C*, Excised wound closed completely with autografts stabilized in place with 5–0 chromic sutures and Steri-Strips. *D*, Sequentially excised and grafted area healed completely as shown on the 28th hospital day.

prevented by frequent rolling, as described below, throughout the first 48 hours of the postoperative period. Grafts of the extremities are usually treated closed and are dressed with compression dressings with circular layers of Kerlix and left dry; or, if a large amount of exudate is expected, they are soaked in 0.5 per cent $AgNO_3$ solution. If a circumferentially grafted extremity is treated "open," the extremity is placed in skeletal traction using Kirschner wires and kept elevated in balanced suspension.

USE OF VIABLE FROZEN SKIN

The number of clinical burn problems for which viable human skin allografts are used has increased during the last few years, resulting in periodic shortages. These shortages of skin grafts have been accentuated by the short shelf-life of human skin even when stored at 4° C. A system of freeze-preservation and long-term storage of viable human skin for periods extending up to several months was developed.[2] This allows great flexibility in the clinical uses of viable human skin grafts. Cadaver skin used as an allograft is harvested when available and stored in the

bank for future clinical need. The bank also provides a mechanism for autograft storage. Occasionally more autograft is harvested than is required to close an excised area. These harvested autografts are prepared, frozen, and stored in a viable state until the next staged excision.

POSTOPERATIVE CARE OF SKIN GRAFTS

The care of skin grafts must avoid graft motion, hematoma, or fluid beneath the graft, and sepsis. "Open" or "closed" techniques are utilized where they best apply in accordance with body area, accuracy of hemostasis, or estimated degree of bacterial contamination.

The difficulty of applying an immobile pressure dressing to the thorax, face, neck, hands, or genitalia favors the open treatment. To maintain intimate continuity of the graft with the wound, fluid or blood accumulation beneath the graft is expressed frequently by "rolling" its exposed surface with sterile cotton swabs from the center to the periphery until the graft is firmly adherent, usually about 48 hours post grafting. Despite the slight motion incurred, this technique is more effective than making stab wounds or "pie-crusting" of grafts, which do not release the fluid completely. Meshed grafts rarely require such "rolling."

Grafted extremities treated openly are elevated by means of transradial or tibial K-wires. By using the closed method, motion and hematoma are minimized by large dressings with external pressure bandages. Whether or not these bandages are saturated with 0.5 per cent $AgNO_3$ depends on the expected extent of wound drainage or the hazard of infection. The interval from operation to primary dressing varies from 3 to 8 days according to clinical signs of infection and the estimate of wound contamination.

During the first postoperative 48 hours, significant hematoma beneath the graft may occur. The graft may still be saved if it is removed, the hematoma evacuated, and the graft replaced. No anesthesia is necessary.

TOPICAL THERAPY WITH 0.5 PER CENT $AgNO_3$

Moyer et al.[13] established that an aqueous solution of 0.5 per cent $AgNO_3$ has an effective antibacterial effect against a wide variety of organisms. In practice copious wet dressings are applied twice daily and saturated with the solution at 2-hourly intervals in order to maintain a constant immersion of the wound.

When exposed to light, $AgNO_3$ turns brownish-black and stains normal skin and the environment. The 0.5 per cent solution is hypotonic and leaches sodium from the blood when applied to raw surfaces.[13] Rare strains of bacteria convert nitrates to nitrites which, when absorbed, convert hemoglobin to methemoglobin. In practice these features limit the use of $AgNO_3$ therapy to patients in the hospital.

Despite imperfections, the 0.5 per cent $AgNO_3$ technique is very versatile when combined with excisional therapy because wounds,

grafts, and donor sites may be included in the same dressing with continuing antibacterial protection. Silver nitrate is not absorbed[7] unless ingested and acts only on the surface of the eschar or wound. It is painless to the patient, and drug sensitivity does not develop. Wound exudate is removed with each dressing, and "tubbing" is not needed. To avoid ingestion and the difficulty of sustained saturation, it is not used on burns of the face.

IMMUNOSUPPRESSION

Immunosuppression is now carried out using antithymocyte globulin. The degree of immunosuppression was monitored by enumerating thymus-dependent lymphocytes in the peripheral blood prior to therapy and 3 times weekly thereafter. This was accomplished by the sheep red blood cell rosetting technique of Wortis.[14] Immunosuppression is continued until the area of unexcised, transplanted allograft is less than 20 per cent of the total body surface.

CROSS-INFECTION AND ENVIRONMENTAL CONTROL

All patients except those with very small burns were housed in the protective environment of the Bacteria Controlled Nursing Unit.[3, 4] This controlled environment provides the patient with a continuous piston-like downflow of bacteria-free air at 90° F and 94 per cent relative humidity, and protects against energy loss as heat of convection and evaporation, as well as airborne cross-infection. The patient is protected against contact cross-infection by clear plastic access walls and by a system of medical care delivery where the medical and nursing personnel do not directly enter the protected environment of the units. Auto infection is reduced by aseptic wound precautions and the use of 0.5 per cent aqueous silver nitrate dressings to the burn eschar until excised, donor sites, and newly grafted areas of the extremities. Patients housed in the Bacteria Controlled Nursing Unit remain in the protective environment until open areas are reduced to less than 5 per cent of the body surface.

NUTRITIONAL MANAGEMENT

Because of the hypermetabolism and wound losses that accompany burns, adequate nutrition becomes the ultimate critical factor for resistance to infection, wound healing, and survival. The patient is weighed daily. Gastrointestinal function reflects abnormalities of general cellular function and is observed closely. Very frequent administration of gastric antacids, the prevention of gastric distention, and the control of sepsis are the most reliable methods to avoid upper gastrointestinal bleeding from stress ulcer or multiple gastric erosions. Gastric distention, vomiting with aspiration, and distention secondary to ileus are controlled by a nasogastric tube. Voluntary oral intake is supplemented by tube feed-

ings administered usually at 2-hour intervals throughout the entire 24-hour period if intake is poor or just during the night if oral intake during waking hours is satisfactory. Adjustment of the volume given in each tube feeding is made in accordance with gastric residuals obtained by aspiration before the feeding. Overloading, hyperosmolarity, or protein intolerance is reflected as diarrhea and requires appropriate adjustments.

Supplemental intravenous hyperalimentation is employed when gastrointestinal function will not satisfy current or projected nutritional requirements. Protocols for positioning of a central intravenous catheter, maintaining electrolyte balance, insulin requirement, and aseptic catheter care are adhered to meticulously. The catheter is removed at once whenever the patient manifests evidence of invasive sepsis.

The metabolic balance of the severely burned patients is maintained carefully throughout the period of open wound by oral and intravenous methods. A minimum daily intake of 3000 cal per m^2 with 3 gm per kg of protein was usually obtained. Malfunction of the gastrointestinal tract, taking the form of gastric retention with ileus or diarrhea, was seen as an ominous sign. Its appearance usually indicated the onset of severe malnutrition and sepsis.

CLINICAL METHODS AND RESULTS

As noted above, for purposes of treatment the patients have been divided into groups according to the size of their thermal injury. Although only deep dermal and full-thickness injury are excised, the total extent of second and third degree burn provides a convenient bench mark for comparison and will be used here. The exact method for the treatment of various size burns is described below.

Children with Burns Up to 44 Per Cent of the Body Surface Area

The primary excision of all deeply burned or devitalized tissue in children with small and medium-sized burns utilized the two excisional techniques and the criteria for the application of each as described above. Children with burn injuries involving less than 45 per cent of the body surfaces allowed straightforward application of the basic principles of excision and wound closure. For practical purposes, the area of unburned skin provided sufficient donor sites to allow immediate closure with autograft. Meshed autograft expanded three to one was used infrequently, and then only in the case of the most extensive excision. In the cases of those patients whose burn area exceeded 30 to 35 per cent of the body surface, conventional donor sites of trunk and extremities often proved insufficient. In these patients the use of the scalp and the feet (areas seldom burned) were used with success in obtaining sufficient donor areas. A 0.5 per cent silver nitrate solution was used, as described in the section on technique prior to excision, and in selected cases postgrafting. In these patients oral alimentation, occasionally supplemented with a gastric feeding tube, was sufficient to provide the required nutritional support.

The Treatment of Large Burns (45 to 75 Per Cent BSA)

Patients with large burn areas present a logistic problem not encountered with smaller burns. Here the amount of unburned skin is insufficient in area to allow primary closure of the entire excised burn wound with autograft.

Although our original concept included partial excision of burns of this size, with an eye towards reducing the area of open burn wound, we have given up this practice, for although it was shown to be effective in selected patients,[9] this has not shortened the burn illness appreciably and leaves extensive areas of burn to spontaneously debride, resulting in a considerable risk of burn wound infection and malnutrition. If the burn wound is to be excised and promptly closed, it is clear that sources of skin other than the patient himself must be utilized. Xenograft and artificial skin have been ineffective in providing long-term physiologic wound closure. Viable cadaver allograft, however, has proved to be as effective as autograft in the closure of primarily excised burn wounds for periods of about 2 weeks. Physiologic wound closure is achieved using viable allograft in exactly the same way autograft is used in skin grafting an open wound.

In the treatment of large burns, therefore, primary excision and prompt wound closure may be achieved initially with a combination of autograft and allograft if the area of allograft wound closure is smaller than the area of available donor site. (For practical purposes, burns up to 65 to 75 per cent are suitable depending on the amount of second degree burn which will heal without grafting.) Continuous wound closure in these patients can be achieved if the "taken" allograft is removed before intense rejection and replaced with autograft.

Fortunately the time taken for a donor site to regenerate for a second cropping is about the same length of time an allograft remains on a wound before rejection. In this treatment system, therefore, it is important to harvest all available donor sites and excise and close the largest possible area of burn wound at the first operative procedure because donor sites begin to heal immediately after cropping. Allografting is carried out at the final excisional procedure to provide complete excision and closure of the burn wound. About 2 weeks after allografting the allografts may be removed easily using the knife handle and, although bleeding is brisk at first, it is easily controlled with pressure alone. Autografting can then be carried out following minor debridement of small areas of the wound where the allograft did not take.

RESULTS OF EXCISION AND PROMPT CLOSURE

In order to evaluate the benefits of excision and closure we compared consecutive series of cases treated by excision, as described above, and those treated with $AgNO_3$ without excision for burns up to 65 per cent BSA.[5] In the past year we have extended these concepts to burns up to 70 to 75 per cent BSA, but the following comparison data do not include burns above 65 per cent.

Table 2. *Complications in Patients Treated*

Complication	$AgNO_3$ Without Excision per cent burn				Excision and Immediate Graft Combined with $AgNO_3$ per cent burn			
	10–19	20–39	40–65	Total	10–19	20–30	40–65	Total
Bacteremia	1	2	3	6	1	2	1	4
Wound sepsis	3	6	10	19	1	5	7	13
Pulmonary complications	3	5	5	13	2	4	3	9
Gastrointestinal bleeding	0	1	0	1	0	1	0	1

The two groups of patients were evaluated in regard to mortality, complications during the acute burn illness, extent of primary excision, period of morbidity (as assessed by the time taken to obtain wound closure), and the clinical result on short-term follow-up.

In analyzing the complications which became manifest during treatment in each of the groups, wound sepsis, bacteremia, and pulmonary complications were predominant. The data regarding these complications, shown in Table 2, are further subdivided according to the size of the injury. The number of complications are in direct relation to the size of the burn. The group treated with primary excision, immediate grafting and silver nitrate therapy had a lower incidence of complications in all categories except gastrointestinal bleeding. Further examination of the data shows that bacterial complications remain the most troublesome, followed by pulmonary complications. Gastrointestinal bleeding was similar in both groups and did not present a frequent clinical problem.

The mortality rate for each group shows that while 4 per cent of the patients undergoing primary excision died during the period of observation, this compares with 11 per cent of those patients receiving silver nitrate alone (Table 3). The most frequent cause of death in both groups was bacterial complications in the form of septicemia, with or without respiratory failure. As might be expected, deaths occurred in those patients whose body surface area burn was the largest. However, patients undergoing primary excision had a lower overall death rate. Further, deaths occurring following this form of treatment were in patients who had an average burn size considerably larger than that seen in patients treated with silver nitrate alone.

The estimate of the overall morbidity suffered by the patient while recovering from a thermal injury is related to the time required to achieve clinical wound closure with functionally satisfactory skin. With that goal as an end point, the two groups can be compared and the effectiveness of the treatment evaluated. In Table 4, the patients are divided into three groups according to the extent of burn. In each group those patients receiving primary excision achieved wound closure in significantly less time than it took the comparable group treated with silver ni-

Table 3. *Mortality in $AgNO_3$ Treated Patients and in Patients Treated with Primary Excision*

	$AgNO_3$ Alone	Excision and Immediate Graft Combined with $AgNO_3$
No. of patients treated	100	100
Per cent who died	11 per cent	4 per cent
No. of patients who died of		
Bacteremia	6	1
Respiratory failure due to pulmonary sepsis	4	3
Brain death	1	0
No. of patients dying in each group separated by burn size		
10 to 19	0	0
20 to 39	4	0
40 to 65	7	4

trate alone. In patients with burns ranging from 10 to 19 per cent BSA, silver nitrate treatment alone required 45 days to achieve functional wound closure while the excised group required 30 days. In the next grouping, patients with burns covering 20 to 39 per cent of body surface area, the silver nitrate group required 75 days for closure; the excision group, 40 days. Finally, in the group whose burns covered 40 to 65 per cent body surface area, the time required using silver nitrate alone was 101 days. In the group treated with excision, 62 days were required for the same result.

In all categories the primarily excised group was improved overall compared with the group treated with topical therapy alone, and the time required to close the burn wound with autograft skin was significantly less than the time required for closure with topical therapy alone. Used as a routine method of treatment, primary excision has not only significantly decreased the hospital stay, as well as morbidity and mortality, but has also markedly reduced the overall pain and psychologic stress that the patient is subjected to during his burn illness. Pain related to

Table 4. *Average Number of Days to Achieve Wound Closure*

	$AgNO_3$ without excision		Excision and immediate grafting and $AgNO_3$	
	No. of Patients	Average No. of Days to Wound Closure	No. of Patients	Average No. of Days to Wound Closure
Per cent BSA				
10 to 19	37	45	40	30
20 to 39	39	75	32	40
40 to 65	13	101	24	62

open wounds and dressing changes is eliminated by wound closure, as are the apprehension and resulting psychologic abnormalities produced by the fear of daily recurrent wound care. These are perhaps the most important benefits to the patient.

BURNS INVOLVING MORE THAN 75 PER CENT OF THE BODY SURFACE

The rapid excision of devitalized skin and prompt grafting present a rational and well supported approach to the problem of extensive skin loss due to burns. However, in the case of massive burns, those covering more than 75 per cent of the BSA with 70 per cent or more of the body involved with a third degree burn, other problems arise. The small amount of unburned skin will only supply split-thickness skin grafts to cover a small portion of the area of skin destroyed immediately after the burn. Furthermore, although allograft may be used to supplement the existing autograft, thus achieving wound closure even in the largest full thickness burn, the duration of allograft wound closure is short. Rejection of allograft, even with tissue matching, takes place in our experience within 12 to 20 days. This is too soon to allow repeated croppings of the patient's donor sites to obtain sufficient autograft to replace the major portion of allograft before rejection takes place and an open wound is produced again. With further modification the method of prompt excision and immediate wound closure may be successful if immunosuppression is used. Such a technique delays rejection of allograft and allows for repeated recroppings of donor sites which in turn allows stepwise allograft excision and closure with autograft, thus preventing the presence of a large open wound at any time post excision.

The concept of immunosuppression and temporary skin transplantation[6] used in the treatment of patients suffering from massive burns differs from renal or other organ transplantation in that permanent survival of the skin allograft is not expected. The essential duration of the transplant is only long enough to allow sufficient time for regeneration of autograft to completely replace the transplanted skin. The term "temporary transplantation" is used to further differentiate this concept from the use of allograft or xenograft skin as biologic dressings in the treatment of burned patients for the short-term protection and preparation of the wound for autografting.

The massively burned patients treated with this technique thus far have been admitted to the Shriners Burns Institute in Boston. Their total burn injury covered 80 per cent or more of the body surface and the area of full-thickness destruction of skin covered 70 per cent or more of the body surface, according to the treatment plan accepted by the Committee on Human Studies. Thirteen patients between the ages of 2 and 11 years, who fulfilled these criteria for massive, full-thickness burn injury, were admitted between March of 1972 and August 1975 and were treated with immunosuppression and temporary skin transplantation. Nine of these patients were discharged from the hospital to return to an active life. The first 11 of these patients are described in

Table 4. The extent of total burn ranged from 80 to 92 per cent of the body surface, and the extent of full-thickness destruction ranged from 70 to 82 per cent of the body surface. The overall mortality was 36 per cent, which may be compared to the mortality of 100 per cent for patients with over 70 per cent BSA full-thickness burns treated by various other regimens in the Massachusetts General Hospital and the Shriners Burns Institute from 1945 to 1973.[6]

In the light of this experience and with the weight of evidence indicating that continuous wound closure following excision of a massive, full-thickness burn would be successful in limiting bacterial and nutritional complications, a treatment plan involving immunosuppression is used taking full advantage of prompt excision of dead tissue and immediate wound closure, the controlled environment of the Bacteria Controlled Nursing Unit, and intensive metabolic alimentation and topical silver nitrate. Skin donors were carefully chosen to provide the closest available tissue type match to the patient. In most cases this was the patient's mother or father. However, in two cases cadaver allograft was used with the usual immunosuppressive regimen without rejection.

Full-thickness burn eschar was excised in a stepwise fashion beginning shortly after admission of the patient. The first operative procedures consisted of harvesting all available donor sites, excising a comparable area of burn (usually a portion of the chest or abdomen), and closing this wound with the harvested autograft. The following three or four procedures consisted of eschar excision and skin transplantation. All areas created by excision were closed in a primary fashion using sheet autograft or allograft 8 to 10/1000 inch in thickness, during the same operative procedure as the excision. The initial operative procedure was carried out on the second or third day post burn, and further operative procedures were carried out every second or third day until the eschar was completely removed and covered with autograft or allograft. Allograft was then excised stepwise as donor sites regenerated and a sufficient amount of autograft became available to graft a substantial area of excised allograft.

SUMMARY

There is much evidence that the most important factor in the successful treatment of skin destruction after thermal injury is to remove dead tissue and promptly close the wound. While the exact methods employed to achieve this goal may vary, in the cases reported here three basic methods were used: (1) simple excision of burn eschar with immediate closure with autograft for small and medium-sized burns; (2) excision and immediate wound closure with autograft supplemented by allograft, with replacement of allograft by autograft before extensive allograft rejection, for large burns; and (3) immunosuppression and temporary skin transplantation for massive third degree burns. All have markedly decreased hospital stay and complications, and in large and massive burns mortality was substantially reduced.

REFERENCES

1. Baxter, C. R.: Topical use of 1.0 per cent silver sulfadiazine. *In* Polk, H. C., Jr., and Stone, H. H. (eds.): Contemporary Burn Management. Boston, Little, Brown & Co., 1971, pp. 217–225.
2. Bondoc, C. C., and Burke, J. F.: Clinical experience with viable frozen human skin and a frozen skin bank. Ann. Surg., *174*:371, 1971.
3. Burke, J. F.: A bacteria controlled nursing unit and individual patient isolation facility. Am. Hosp. Assoc., Int. Conf. on Nosocomial Infections, 1971, p. 216.
4. Burke, J. F.: Isolation techniques and their effectiveness. *In* Polk, H. C., Jr., and Stone, H. H. (eds.): Contemporary Burn Management. Boston, Little, Brown & Co., 1971, pp. 141–150.
5. Burke, J. F., Bondoc, C. C., and Quinby, W. C., Jr.: Primary burn excision and immediate grafting: A method shortening illness. J. Trauma, *14*:389, 1974.
6. Burke, J. F., Quinby, W. C., Bondoc, C. C., et al.: Immunosuppression and temporary skin transplantation in the treatment of massive third degree burns. Ann. Surg., *182*:183, 1975.
7. Constable, J. D., Morris, P. J., and Burke, J. F.: Absorption pattern of silver nitrate from open wounds. Plast. Reconstr. Surg., *39*:34, 1967.
8. Cope, O., Laugohr, J., Moore, F. D., and Webster, R.: Expeditious care of full thickness burn wounds by surgical excision and grafting. Ann. Surg., *125*:1, 1947.
9. Hendren, W. H., Constable, J. D., and Zawacki, B. E.: Early partial excision of major burns in children. J. Ped. Surg., *3*:445, 1968.
10. Huggins, C., Suzuki, H., Warford, H. E., et al.: 2,3-diphosphoglycerate in frozen blood. Proceedings of 23rd Annual Meeting, Am. Assoc. of Blood Banks, 1970, p. 112.
11. Lewis, R. J., and Quinby, W. C., Jr.: Electrosurgical excision of full-thickness burns. Arch. Surg., *110*:191, 1975.
12. Moncrief, J. A., Linberg, R. B., et al.: Use of topical antibacterial therapy in the treatment of the burn wound. Arch. Surg., *92*:558, 1966.
13. Moyer, C., Brentano, L., et al.: Treatment of large human burns with 0.5 per cent $AgNO_3$ solution. Arch. Surg., *90*:812, 1965.
14. Wortis, H. H., Cooper, A. G., and Brown, M. D.: Inhibition of human lymphocyte rosetting by anti T sera. Nature, *243*:109, 1973.

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Reconstructive Surgery for Major Craniofacial Deformities

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Although craniofacial surgery of increasing complexity has been performed since World War II, the decisive factor in the current worldwide application of craniofacial surgery is Tessier's development of a surgical approach to a previously inaccessible area. This allows exposure, dissection, and repair of practically every type of facial deformity, whether congenital, traumatic, or neoplastic in origin.

The experience at Children's Hospital Medical Center and Peter Bent Brigham Hospital since 1955 includes over 400 patients with a variety of craniofacial defects and shows a gradual increase in complexity of problems treated. In 1970 a major change in evaluation and therapy occurred because of Tessier's contribution. The earlier experience was more standardized for defects of congenital clefts of lips and palates, mandibular and maxillary dysostoses, and orbital neoplasms; currently, treatment is more flexible and adaptable for almost every variety of deformity. The earlier work required collaboration only of a plastic surgeon and orthodontist; present activity requires participation by neurosurgery, ophthalmology, radiology, anesthesiology, speech and hearing, and psychosocial disciplines.

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Figure 1. At 5 years of age patient M. M. had craniectomy for synostosis. At age 16 years she had midface advancement, Le Fort III. Eight months later she had osteotomy of mandible and rhinoplasty. She is now 2 years post surgery, is a National Merit Scholar, and plans on entering college. *A*, Preoperative anteroposterior view of full face shows mild exorbitism, sunken cheeks, and maxillary hypoplasia. *B*, Two years after surgery eyes appear normal, cheeks are convex, and dental occlusion is excellent. *C*, Preoperative lateral view shows flattened cheeks and long chin. Hair is styled to cover face as much as possible. *D*, Postoperative lateral shows harmonious appearance of eyes, cheeks, nose, teeth, and chin. Hair style reveals full face.

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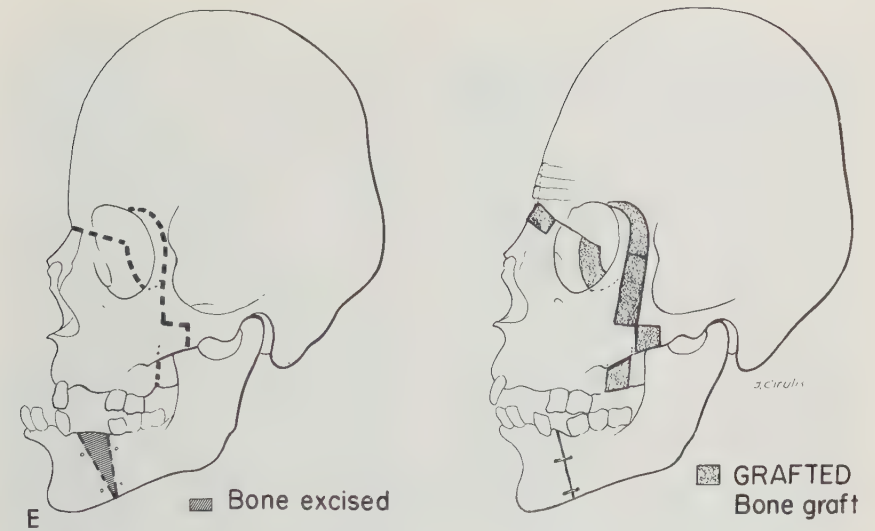

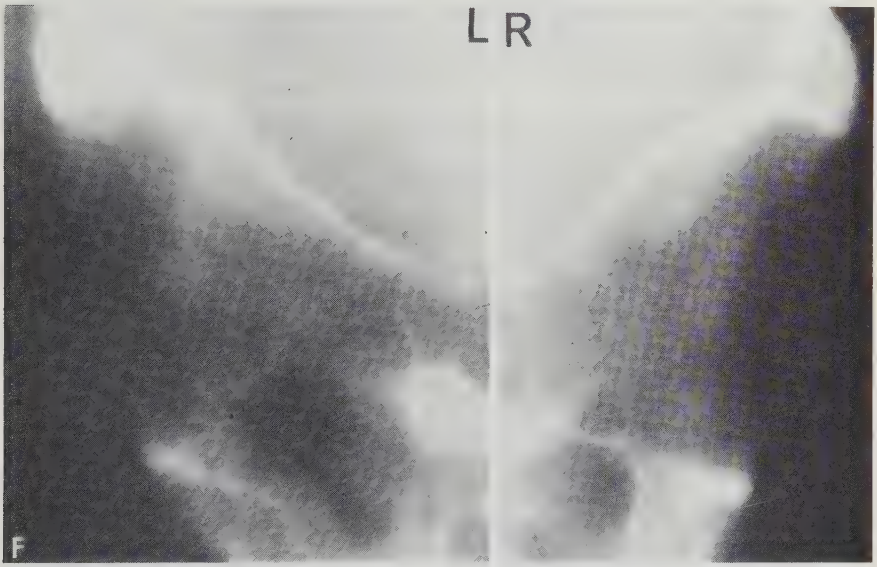

Figure 1 *Continued.* *E,* Sketch shows osteotomy sites (left drawing, dotted lines) along nasal, frontal, zygomatic, and maxillary bones. V-resection of body of mandible (left drawing, shaded) was performed 8 months after midface advancement. Rhinoplasty osteotomies not shown. On right drawing the shaded area shows sites of bone graft replacement. Main support comes from bone blocks at root of nose, lateral orbital walls, zygomatic arches, and behind maxillary tuberosities.

F, Lateral tomography of the orbits parallel to the midorbital vertical plane. The orbital roofs clearly extend far beyond the level of the orbital floors which are poorly developed in association with the maxillary hypoplasia. By measurement the maxillary retrusion with respect to the inferior orbital margins is 11 mm on each side. The superior aspect of the orbits is regarded as normal on each side and the lesion is referable to the maxilla.

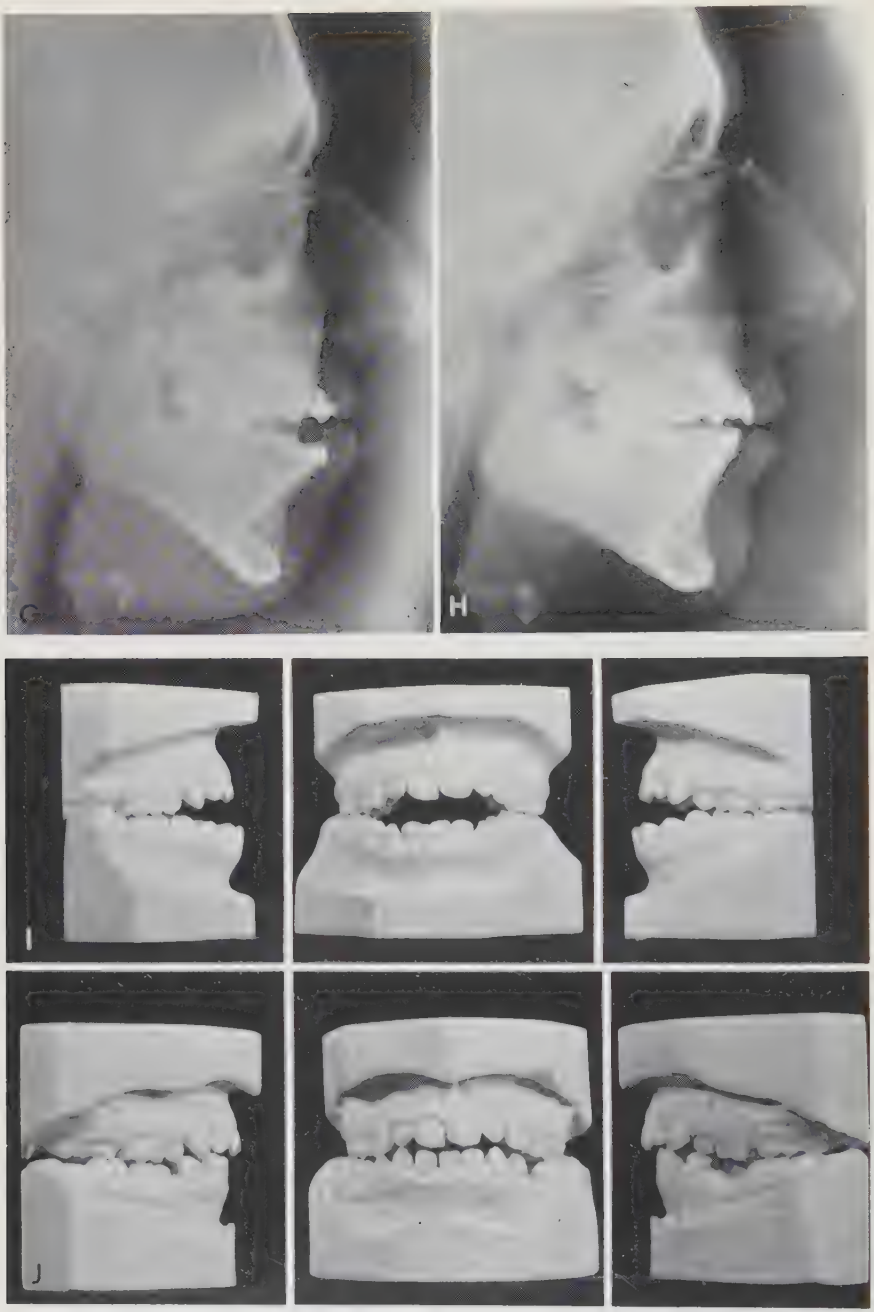

Figure 1. *Continued.* *See legend on the opposite page.*

PREOPERATIVE CONSIDERATIONS

Each patient is seen by the plastic surgeon and orthodontist with referral for appropriate consultation. The baseline studies in addition to regular medical assessments include a study of patterns of growth and intellectual development. The ophthalmologic exam includes measurements of visual acuity, visual fields, colored vision, eye position, muscle movement, and funduscopic study. The most accurate measurement of the distance between the eyes is by x-ray, the site of measurement to be determined by the anteroposterior and basal tomograms. The senses of taste and smell are also tested.

MIDFACE STENOSIS

M. M., CHMC #78–19–25, female, born April 16, 1957, diagnosis Crouzon's disease. At age 5 years the patient underwent craniectomy and at age 6 and 7 she had operations for stenosis of the ear canals. She was first seen in January, 1973 at CHMC regarding malocclusion and exophthalmos. Evaluation revealed normal intelligence (a National Merit Scholar), general good health, marked maxillary underbite with distorted mandibular horizontal occlusal plane, shallow cheeks, exophthalmos, normal vision, and normal airway (Fig. 1, *A* and *C*). She was evaluated by neurosurgery, ophthalmology, dentistry, otolaryngology, and by x-ray polytomography. Lateral x-rays reveal shallow infra-orbital margins, a sunken middle of the face, marked maxillary underbite, and the depressed anterior segment of the mandible (Fig. 1*F*).

Possible methods of treatment included the following, either alone or in combination: (1) mandibular osteotomy with superior and posterior displacement of the body of the mandible; (2) horizontal maxillary osteotomy above the alveolus (Le Fort I) with advancement of the maxilla with or without onlay bone grafts to the anterior maxillary walls; (3) midface advancement (Le Fort III) to advance as a unit the nose, the inferior orbital rims, and the mandible; (4) rhinoplasty.

The decision was made after study of the x-rays, dental models, and photographs and discussion with the patient and family to perform the Le Fort III to achieve basic symmetry of the forehead, nose, cheeks, and upper jaw (Fig. 1, *G* and *H*). After this was solidly healed, a planned osteotomy of the body of the mandible and a rhinoplasty were to be done.

The midface advancement was performed in June, 1973; intermaxillary fixation was maintained for 8 weeks (Fig. 1*E*). In February 1974

Figure 1 *Continued.* *G*, Lateral cephalometrogram after midface advancement shows improved position of orbits and maxilla. Note that maxilla was purposefully not tilted inferiorly to make contact with mandibular incisors. If this had been done, entire midface would have been elongated. *H*, Lateral cephalometrogram after V-resection of body of mandible and rhinoplasty. Note excellent occlusion and harmonious relationships of orbits, nose, teeth, and chin.

I, Preoperative views of dental models show open bite and the slanting occlusal surface of anterior mandible. *J*, Postoperative views of dental models show excellent functional relationship of upper and lower dentitions. (All figures reproduced from Ann. Surg., *182*:240–265, 1975. Used with permission.)

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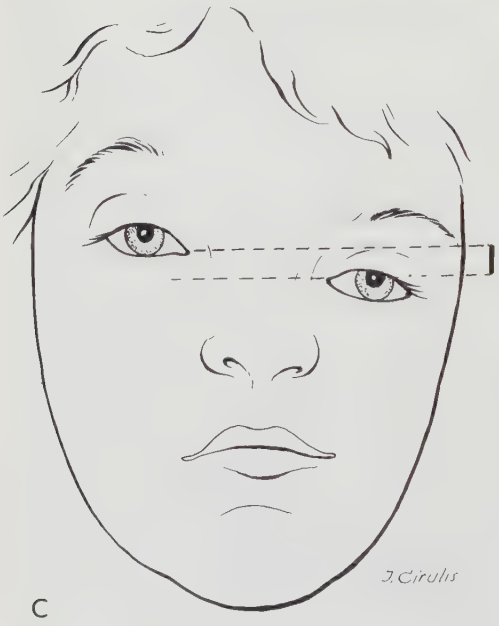

Figure 2. An 8-year-old girl with cranial synostosis corrected at age 6 weeks. Currently she has mild orbital hypertelorism with asymmetry of level of orbits. Occlusion satisfactory. *A*, Preoperative view shows elevation of right orbit and eye with posterior displacement of lateral wall and roof. Note bifid nose. *B*, Six months postoperatively, orbits are level and 12 mm closer together. Nose is narrowed. Scars are fading rapidly. *C*, Preoperative sketch showing difference in levels of orbits.

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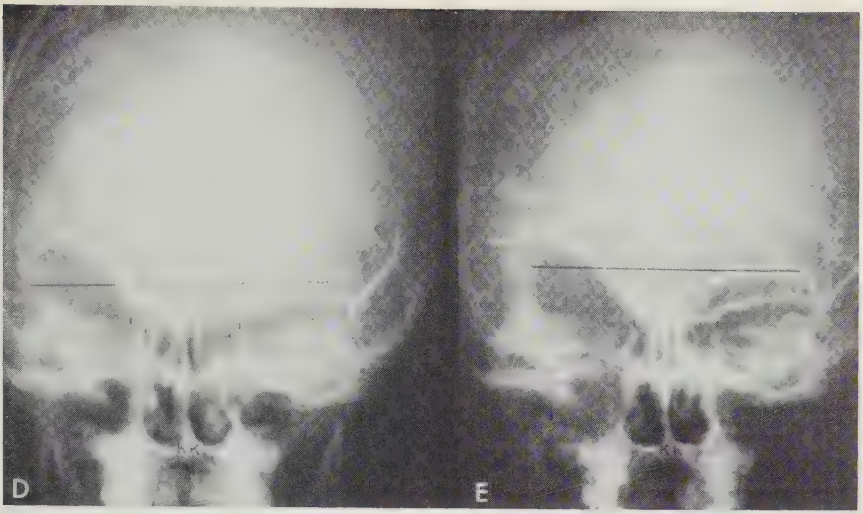

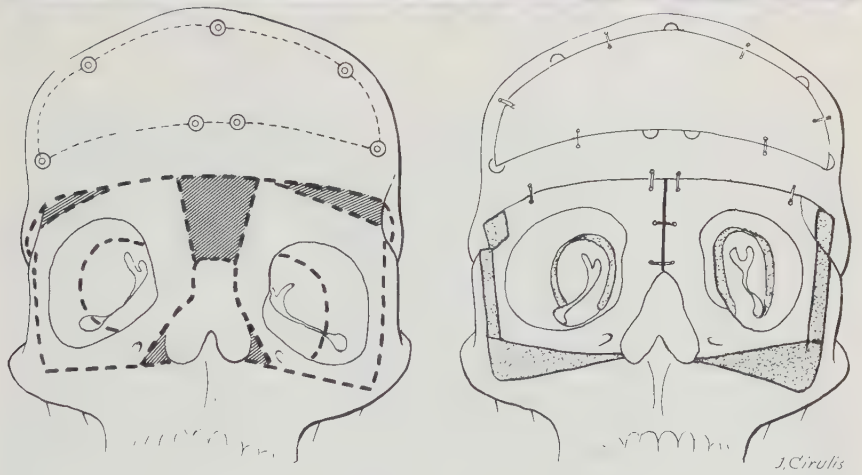

F

Bone excised GRAFTED Bone graft

Figure 2 *Continued.* *D*, Preoperative posteroanterior view of the skull. What appears to be the broader interorbital distance, marked by the more lateral of the short black marking pairs, is probably the interorbital distance at the midorbital level, whereas the two small markers that are more medially placed are regarded as representing the more anterior margins of the lacrimal bones. It is the more narrowed dimension that is the one that corresponds to the clinical assessment and the one that should be recorded in measuring the degree of hypertelorism. In the patient there was also right coronal synostosis with an elevation of the right sphenoid ridge and right superior lateral orbital margin. The solid black line is drawn on the level of the normal left superior orbital rim. *E*, Postoperative posteroanterior skull. The interorbital distance as far anteriorly as can be seen has been reduced to 18 mm, corrected for distortion, and the discrepancy in the level of the orbital roofs has been reduced by the placement of bone grafts in the superior lateral aspect of the right orbit (not well seen on print).

F, Sketch of operative osteotomies and bone grafts. Frontal bone flap is removed by neurosurgeons to give access to floor of frontal fossa. Horizontal strut of frontal bone is left intact as support for osteotomized orbits. Bone excised (left drawing) included 14 mm of frontonasoethmoid complex as a unit. Other bone excisions were required to allow symmetrical fit after migration of mobilized bony orbits. Bone grafts (right drawing) are placed in lateral orbital walls, maxilla, and above right orbit.

the osteotomy of the mandible was performed, and during the same hospitalization the rhinoplasty was done. The patient did well. She was hospitalized 10 days after the first operation and 7 days after the second operation. She has had no complications and will enter college this fall (Fig. 1, *B*, *D*, *I*, and *J*).

This patient illustrates factors in selection of operation. She also had a greater maxillary underbite than the relationship of the incisor teeth suggests because the maxillary incisors are tilted anteriorly in an effort to compensate for the gap between them and the mandibular incisors. If surgical correction were planned merely to obtain proper relationship of the incisor teeth, the midcheek areas would still have been shallow and posteriorly displaced and the exophthalmos would not have been corrected.

HYPERTELORISM

K. K., CHMC # 78–96–39, female, born July, 1966. The patient had a craniectomy at age 6 weeks and was followed elsewhere. She was referred in December, 1973 because her parents stated that the child had long desired an operation to correct the facial deformity. Examination revealed good general health. There was moderately severe hypertelorism with asymmetry of the forehead, a bifid nose, a right parietofrontal bony defect, with the right orbit higher than the left, and normal dental occlusion (Fig. 2, *A* and *C*). Ophthalmologic examination revealed astigmatism, nystagmus, and alternating heterotropia. On looking at a distance the eyes were divergent with right hypertropia. X-ray revealed that the right orbit was asymmetrical and elevated (Fig. 2*D*). The inner canthal distance measured 30 mm. There was absence of the right frontal sinus. It was difficult to determine which side was the normal.

A bifrontal craniotomy was performed but after removal of the frontal bone flap, unexplained hypotension and cardiac arrhythmias occurred lasting for 45 minutes. It was felt wiser to discontinue the surgery rather than proceed with these unexplained hemodynamic changes. The patient was discharged from the hospital and readmitted for the second operation June 13, 1974. At this time the incisions were reopened and the bony osteotomies performed as outlined in Figure 2*F*. The right orbit was lowered by 4 mm (Fig. 2*E*).

Fourteen millimeters of bone in the frontonasal ethmoid area were excised and the bony orbits sutured together in the midline. It was difficult even at surgery to identify the normal midline. This was finally settled by drawing a line between the frenulum and the incisor teeth and up through the nasal spine, then selecting a line at right angles to it in the forehead area. In advancing and rotating the right orbit we were able to correct the fall-off in the lateral orbital plane. A nasal bone graft was also placed and appropriate skin excised and a Z-plasty performed. Bilaterally inner canthoplasties were also performed.

The patient made an excellent recovery and was discharged on the 10th postoperative day. Since then there have been no problems; the scars are fading well (Fig. 2*B*). She has normal taste and smell.

This patient illustrates the flexibility of the surgical approach. The hypertelorism per se, although minimal, was definite and seemed accentuated by asymmetry of orbits. The child herself was aware of the defect and asked for correction. The parents were intelligent. Serious preoperative difference of opinion existed within our craniofacial group regarding the advisability of surgery for this patient. The final decision was based on a balance between the dangers of the surgery and the desire to help the patient.

Other varieties of hypertelorism lend themselves to surgical correction. In Figure 3*A* we have a teenaged patient with hypertelorism and an encephalocele. This patient was trainable and educatable but not in the range of completely normal intelligence. It was extremely difficult preoperatively to determine just where the midline was. Only after careful study of the photographs, the patient, and the x-rays did we decide to perform a unilateral left-sided orbital osteotomy. The left orbit was migrated medially 35 mm and wired to the opposite nasofrontal ethmoid bone. Bone grafts were placed on the pre-existing frontal bone defect as well as in the operatively created lateral orbital wall defect. A scalp flap was rotated to the forehead area to cover the bone grafts. Sub-

Figure 3. *A*, Patient is a 21-year-old girl with large pulsating bony defect in right forehead secondary to frontonasal encephalocele repair. Pedicle flap had been removed from forehead to repair nose. Only after study of x-rays, dental models, and photos did we decide to do left orbital osteotomies leaving right side intact. *B*, Patient has had two operations. First was to move left orbit 35 mm medially with bone grafts to lateral orbit, forehead, and zygoma. Hair-bearing scalp pedicle flap was required to cover bone grafts. Photo was taken 3 weeks after second operation at which hair-bearing scalp was replaced by skin graft. Attempted use of patient's original eyebrow as a flap for better brow alignment failed.

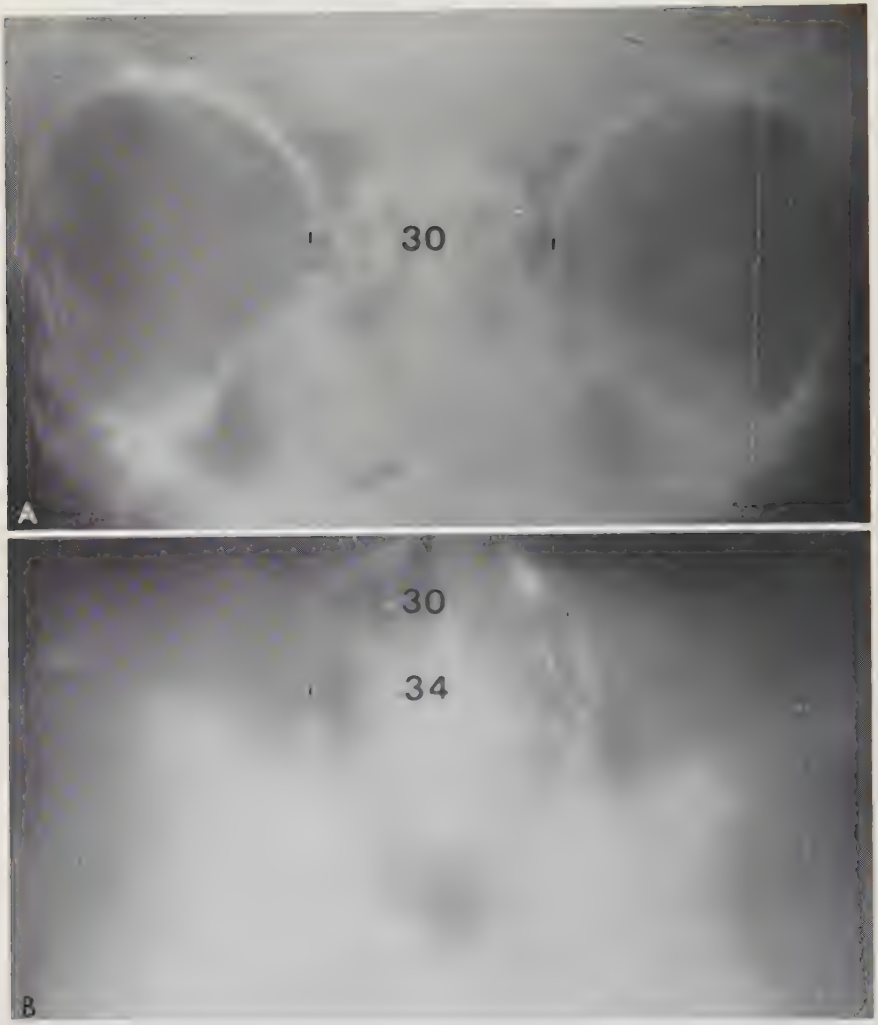

Figure 4. *A*, Frontal or coronal plane tomography through the orbits far anteriorly. The interorbital distance measures 30 mm corrected for magnification. *B*, Base or horizontal tomography at the midorbital level. The level at which the above 30 mm measurement was determined can readily be seen and localized as being at the anterior extreme of the lacrimal bone, probably very close to the posterior lacrimal crest at the midorbital level. The ethmoid sinuses are fusiform in shape so that a measurement halfway back into the orbital cone would have an interorbital distance of 34 mm. The most anterior margins of the lacrimal bone that can be identified are the ones used in measuring the degree of orbital hypertelorism.

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Figure 4 *Continued.* *C-F,* Pre- and postoperative anteroposterior and lateral views of patient. Note preoperative flattening of entire face in AP dimension. Forehead and nose have been brought forward with bone grafts. Orbits were migrated medially 14 mm. This should be contrasted with preoperative anteroposterior view in Fig. 4*A*.

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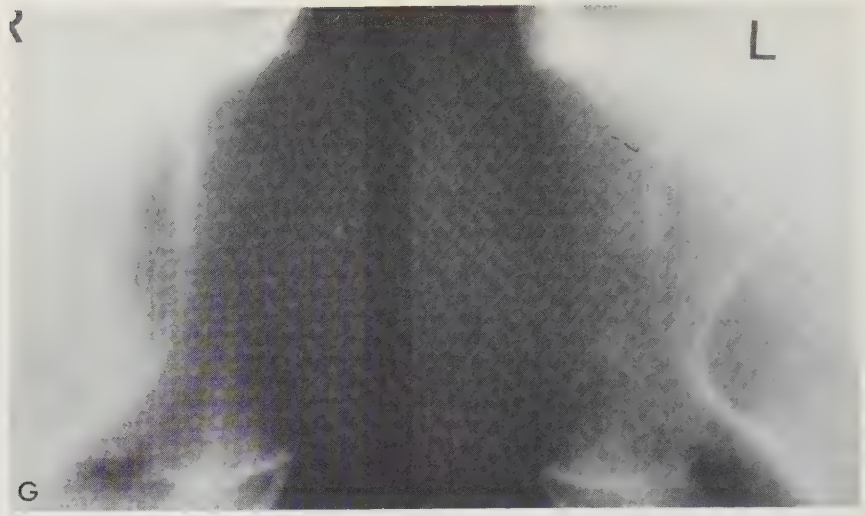

Figure 4 *Continued.* *G*, Right and left orbital tomography parallel to the vertical midorbital plane. Again, the protrusion of the middle cranial fossa into the orbital spaces can be appreciated. Perhaps as a form of compensation, the orbits appear to have an increased vertical dimension as well as being very shallow.

sequently the hair-bearing portion of the scalp has been excised and replaced with a split-thickness skin graft (Fig. 3*B*). Incidentally, at the original operation this patient had a calcified falx cerebri which caused a difficult prolonged dissection for the neurosurgeon in raising the frontal bone flap. Therefore, repair was staged and the osteotomies and bone grafts were performed 1 week later.

Another patient with hypertelorism demonstrates flattened, anterior-posterior dimensions of the entire face and is therefore a different type of problem for analysis (Fig. 4, *A-F*). Note on x-ray the shallow orbits with the short orbital floors and roofs (Fig. 4*G*). Also note the anterior displacement of the greater wing of the sphenoid, indicating the forward projection of the temporal lobes of the brain. This child had been rejected by his mother early in life and was brought up by a devoted grandmother who for 10 years had been seeking someone, somewhere, who could help correct this child's deformity.

This patient's problem was corrected with a one-stage operation; hospitalization was 12 days, with no complications. He states that his schooling is much more pleasant for him since the surgery, and he and his family are extremely satisfied.

TREACHER-COLLINS

E. W., CHMC #60-14-38, male, born June 6, 1964. This 9-year-old boy was referred from a genetics study group after his parents had sought correction of the defect ever since birth. The child was of normal intelligence and had normal vision, normal occlusion, and normal breathing. His deformity was chiefly in the shape of the eyes and the

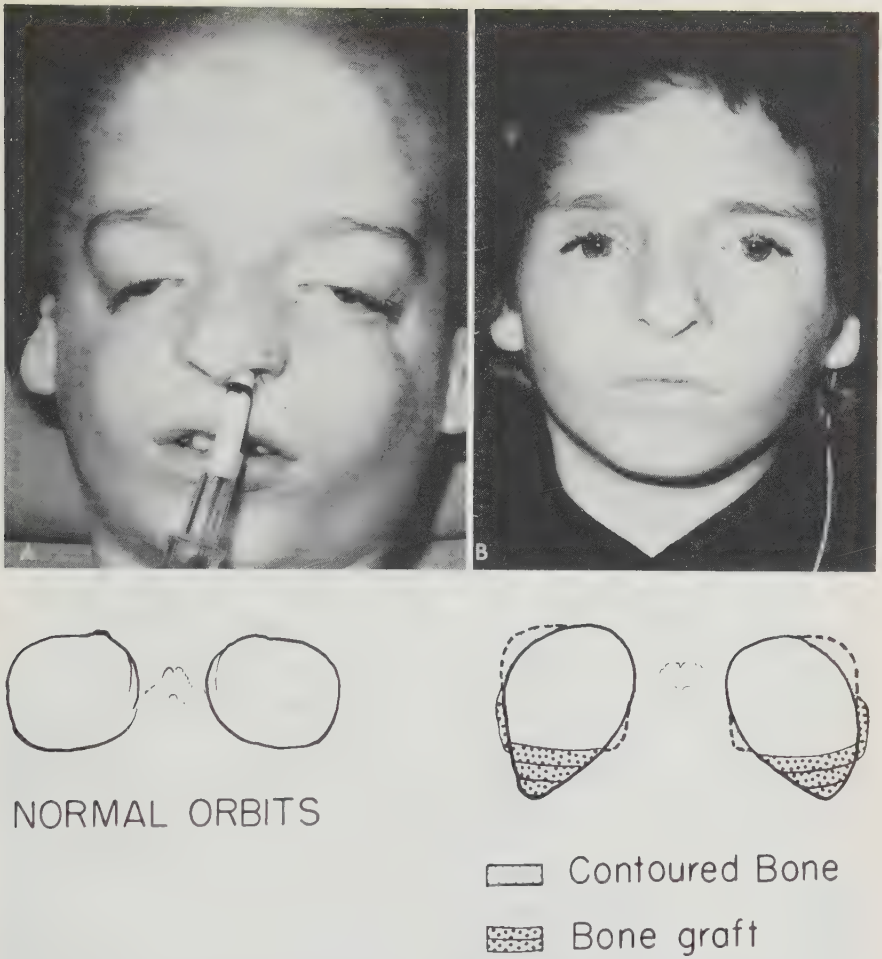

Figure 5. *A*, Nine-year-old boy with Treacher-Collins syndrome. Note coloboma of lower eyelids, depression of cheeks, and antimongoloid slant to orbits. *B*, Postoperative correction obtained with onlay bone grafts to lateral orbital walls, elevation of lateral portion of orbital floors, and contouring at superior lateral angle. Zygomatic arches reconstructed with continuous split rib grafts. *C*, Sketch of outline of normal orbits (left) compared to postoperative sketch after onlay bone grafts and contouring of upper outer angle.

orbits with coloboma of the lower eyelids, antimongoloid slant to the orbits, and deficiency of the cheeks (Fig. 5*A*). Hearing was impaired but correctable with a hearing aid.

After complete evaluation surgical correction was performed on January 10, 1974. Three ribs were removed, split, and used for grafts to the zygomatic arches and the roof, lateral wall, and floor of the orbits (Fig. 5*C*). The overhanging superior lateral angles of the orbits were burred away to create a near normal squared appearance of the bony orbits. The zygomatic arches were reconstructed with a continuous split rib graft wired to the zygomatic process of the temporal bone laterally and into the anterior maxillary wall medially.

Figure 6. *A*, Seven-day-old baby with massive carcinoma invading mandible. *B*, Same child at 3 years of age following surgical excision and x-ray therapy; note defect on left side of face. *C* and *D*, Same patient shown at age 12 has had no evidence of tumor. Defect is surprisingly similar to that of hemifacial microsomia with depression of soft tissues, shortened mandible, and deviation of jaw opening. *E*, Intraoperative photo shows reconstruction of zygomatic arch, total reconstruction of temporal fossa, interpositional bone graft between newly made fossa and remnant of body of mandible. Silastic capping of bone strut, and onlay grafts over entire mandible to produce angle and body. *F*, 1 = onlay split rib bone graft to reinforce zygomatic arch and provide accentuation of glenoid fossa; 2 = Silastic membrane for joint surface and to prevent fusion; 3 = reconstructed ramus portion of mandible; 4 = onlay split rib bone graft for reinforcement and additional contour; 5 = vestigial coronoid process of right side of mandible; 6 = body of mandible. *G*, Two months after surgery, patient has much improved contour and function.

Figure 6 *Continued.* *See legend on the opposite page.*

There was an excellent result (Fig. 5*B*). The patient was hospitalized for 8 days. He developed trismus requiring operative forced opening of his jaws on August 26, 1974. Since then he has done well.

This patient illustrates the correction of a defect with onlay grafting without the need for osteotomies. Prior to Tessier's contribution, correction of these defects was never satisfactory and consisted merely of attempted soft tissue or prosthetic contouring of the cheek. Now by observing these defects directly, surgeons can develop a new insight into the embryologic processes leading to the development of the temporal bone and the relationship of the zygomatic processes to the temporal bone, the middle ear, the orbit, and maxilla. The ability to observe and record these defects in a human is directing and influencing analysis of primate embryology and suggesting ways for future investigation.

TUMOR

M. M., CHMC #54-54-70, female, was born November 25, 1962. This patient had a duct cell carcinoma of the parotid gland present at birth with invasion of the mandible (Fig. 6*A*). On December 11, 1962 the carcinoma was excised followed by chemotherapy and x-ray therapy (Fig. 6*B*). There was no recurrence.

She was next referred at age 12 for re-evaluation of the deformity which interestingly resembled that of a hemifacial microsomia. The zygoma was undeveloped, the mandibular ramus absent, and the body of the mandible small. All soft tissues were atrophic and an obvious concavity of the left side of the face existed (Fig. 6,*C* and *D*).

After evaluation repair was performed and consisted of reconstruction of left zygoma, left temporal fossa, left ramus, and body of the mandible with additional onlay bone grafts along the body of the mandible. The total reconstruction was therefore a one-stage repair of the zygomatic arch and temporomandibular joint along with the body and ramus of the mandible (Fig. 6,*E* and *F*). The effect on facial symmetry was satisfactory, in addition to the functional improvement in her chewing and speaking (Fig. 6*G*). The patient's hospitalization was 15 days, the course prolonged by the complication of pneumothorax which required thoracic tube drainage for 8 days.

In our experience this is a unique tumor; microscopic diagnosis was verified as adenocarcinoma of duct cell origin. It is impossible to distinguish between the effects of the surgery and of the x-ray therapy in the causation of the defect but its similarity to hemifacial microsomia is striking.

DISCUSSION

Advances in treatment for craniofacial defects have increased interest and enthusiasm, for clinicians at least, in the embryology and genetics of congenital defects. Several recent conferences have been

devoted to this subject.[1-7] Repair of the congenital deformity does not solve the child's or the parent's multiple problems since associated anomalies and side effects may remain and cloud the patient's future. The study of congenital abnormalities may provide clues to etiology and prevention. Although progress has been made in recognition and cataloguing of syndromes, difficulties still overwhelm us in delineation, classification, and terminology. Etiology is all the more elusive.

The general classifications used for our patients were selected to give some order to therapy. Analysis of the defects is required in order to plan selectively for appropriate treatment for the individual patient. The term "orbital hypertelorism" means abnormally wide distance between the eyes and is a finding secondary to encephalocele or other cranial or facial clefts or premature synostoses. It may be confused with telecanthus, a lateral displacement of the inner canthi, or exotropia leading to wide interpupillary distance. Premature synostoses of the cranial sutures have been divided conveniently by Converse into three groups: simple cranial synostoses, craniofacial dysostoses (Crouzon's disease), and acrocephalosyndactyly (Apert's syndrome). Shillito estimates approximately 10 per cent of patients with craniostenosis show significant facial deformity.

Many patients are referred after well meaning but unrealistic reconstructive surgery. To repair surface defects without correcting the fundamental bony malformation can make much more difficult a proper definitive reconstructive procedure.

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REFERENCES

1. Bergsma, D., (ed.): Malformation Syndromes. The National Foundation, Intercontinental Medical Book Corporation, Vol. X, No. 7, 1974.
2. Converse, J. M., Wood-Smith, D., McCarthy, J. G., and Coccaro, P. J.: Craniofacial surgery. Clin. Plast. Surg., *1*:499–557, 1974.
3. Converse, J. M., Wood-Smith, D., and McCarthy, J. G.: Report on a series of 50 craniofacial operations. Plast. Reconstr. Surg., 55:3, 1975.
4. Jabaley, M. E., and Edgerton, M. T.: Surgical correction of congenital mid-face retrusion in the presence of mandibular prognathism. Plast. Reconstr. Surg., 44:1, 1969.
5. Munro, I. R.: Orbito-cranio-facial surgery: The team approach. Plast. Reconstr. Surg., 55:2, 1975.
6. Murray, J. E., and Swanson, L. T.: Mid-face osteotomy and advancement for craniosynostosis. Plast. Reconstr. Surg., *41*:299, 1968.
7. Shillito, J.: Premature craniofacial synostoses. Neurosurgical treatment. *In* Proceedings of International Conference on Diagnosis and Treatment of Cranio-facial Anomalies, October 25–28, 1971. St. Louis, C. V. Mosby Co., in preparation.

8. Tessier, P.: The definitive plastic surgical treatment of the severe facial deformities of craniofacial dysostosis. Crouzon's and Apert's disease. Plast. Reconstr. Surg., *48*:419, 1971.
9. Tessier, P.: Orbital clefts and Treacher-Collins syndrome. Symposium on Surgery of the Orbit. Dallas, Texas, 1974.
10. Tessier, P., Guiot, G., Delbet, J. P., and Pastoriza, J.: Osteotomies cranio-naso-orbito-faciales hypertelorisme. Ann. Chir. Plast., *12*:103, 1967.
11. Willmar, K.: On LeFort I osteotomy. Scand. J. Plast. Reconstr. Surg., Supplementum 12, 1974.

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Current Management of Childhood Solid Tumors

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A significant improvement in survival of children with embryonal malignancies has been achieved in the past decade. The most important factor influencing these results has been the use of aggressive combined treatment including operative extirpation, regional radiation therapy, and prolonged courses of chemotherapy. Other key factors that have influenced improvement in survival have been an appreciation of the natural history of specific tumors by retrospective and prospective case analysis from multi-institutional cooperative group studies, appropriate staging procedures to accurately determine the extent of disease, and prompt referral of patients with suspected or confirmed neoplasms to pediatric cancer centers experienced in the treatment of childhood neoplasia. This report describes a current plan of management for a number of commonly encountered childhood solid tumors.

NEUROBLASTOMA

Neuroblastoma may arise anywhere along the sympathetic ganglion chain from the stellate ganglion in the neck to the pelvic organs of Zuckerkandl, as well as in the adrenal medulla (Fig. 1). This neoplasm often has a bizarre behavior with no similar counterpart observed in adult cancer patients. Occasional reports have been recorded concerning spontaneous cures and maturation from malignant to benign forms. These unusual neurogenic tumors produce excess circulating catecholamines which can cause hypertension. High levels of catecholamine deg-

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Figure 1. Neuroblastoma of neck (*arrow*) in a 4-month-old treated by 90 per cent subtotal resection and x-ray therapy resulting in long-term cure.

radation products excreted in the urine make the 24-hour VMA and HVA urine determinations a valuable diagnostic test. One or both of these metabolites are elevated in the majority of cases (greater than 85 per cent) when expressed as μg VMA per mg creatinine (normal $<$ 20 μg/mg). The embryonal nature of this tumor is well documented by its occurrence in the neonate. Instances of actual involvement of the maternal placenta at the time of delivery have been reported.

Children with neuroblastoma may present with varied constitutional symptoms including weight loss, fever, anorexia, anemia, and leg pain or a black eye from osseous extremity or orbital metastases. Gastrointestinal manifestations such as diarrhea are also observed. In recent years, 2 per cent of affected children have presented with unusual neurologic manifestations such as polymyoclonic ataxia with or without opsiclonus and severe nystagmus.[20, 22] While these patients have an improved survival (90 per cent), neurologic symptoms often persist despite resection of the tumor. Patients with mediastinal neuroblastoma often present with respiratory distress due to tracheal and or lung compression by a space-occupying lesion. Paraplegia may be observed as a result of dumbbell-shaped tumor extension through an intervertebral foramen causing extradural cord compression. Peculiar gait due to iliopsoas spasm is seen in instances of paraspinal retroperitoneal neuroblastoma. The most frequent presenting finding however, is the presence of a large, firm, nodular, and sometimes painful flank mass.

The tumor often shows fine diffuse calcification on plain abdominal x-ray. In children with adrenal neuroblastoma, the intravenous pyelogram usually demonstrates an extrinsic downward or lateral displacement of the ipsilateral kidney. Paraspinal lesions usually show lateral displacement of kidneys or ureters (Fig. 2*A*). An inferior venacavagram is done at the same time the IVP is obtained, and may show venacaval obstruction with collateral venous circulation via the paravertebral venous plexus (Fig. 2*B*). As bone is the most common site of spread of neuroblastoma, bone marrow aspirate, metastatic bone survey, and radioactive pertechnetate diphosphonate bone scan should be obtained routinely. The bone scan appears to be more sensitive in detecting early osseous metastases, but can also be positive in patients with recent bone trauma or inflammation. Platelet count, prothrombin time, and partial thromboplastin time should be obtained as these may be abnormal due to bone marrow and liver involvement.

The neoplasm has been staged into four groups:[6] Group 1 refers to localized tumor without extension that is completely excised (10 per cent of cases). Group II refers to a tumor with extension to regional lymph nodes, but which is completely resected (15 per cent of cases). Group III refers to a tumor (usually large) that crosses the midline and is incompletely removed or simply biopsied (25 per cent of cases). Total excision is often initially impossible in Stage III cases because the tumor frequently envelops major vessels, the bowel mesentery, or extends across body cavities. Group IV patients have distant metastases (particularly to bone cortex) and have a grave prognosis. Unfortunately, more than 50 per cent of cases of this highly malignant tumor have metastasized at the time of initial diagnosis.[11]

An additional and unique group of patients classified as IV-S are cases that present in infants usually under the age of 1 year with liver metastases, subcutaneous tumor nodules, and bone marrow involvement without bone cortex involvement (Fig. 2*C*). We have observed a 75 per cent survival in these cases with a variety of treatment methods. Evans et al. have similarly reported good results (84 per cent survival rate) in these unusual patients.[4] Death in these infants is usually unrelated to the tumor, but rather due to respiratory insufficiency from diaphragmatic elevation by a huge liver filled with tumor or from sepsis. Schnaufer and Koop have reported the creation of a temporary ventral hernia using Silastic sheeting (much like treatment of neonates with abdominal wall defects) to relieve intra-abdominal pressure in two cases.[21] One patient survived this treatment, and the other succumbed from sepsis. IV-S survivors show a slow but gradual disappearance of these multiple sites of metastatic tumor over a 6 to 12 month period with or without therapy.

Therapy of choice in Stage I, II, or III lesions is total excision of the primary lesion and any local extension of disease. While this is feasible in many Stage I and II cases, lack of a true capsule and paraspinal or intraspinal extension can make total excision impossible. The fact that neuroblastoma is quite radiosensitive makes x-ray therapy an attractive adjunctive treatment method, while surgery alone is probably accept-

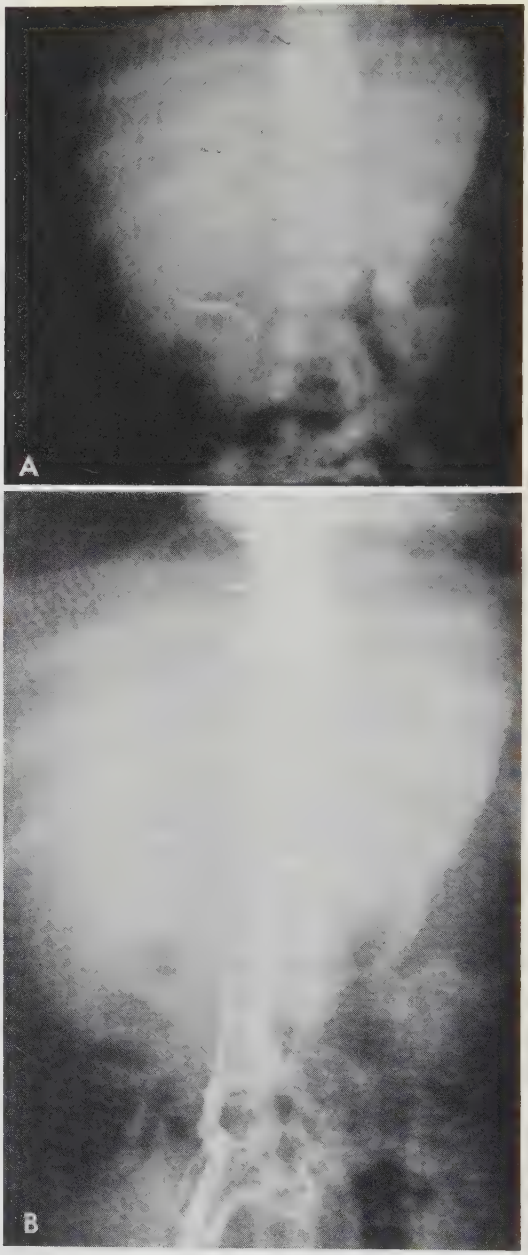

Figure 2. *A*, Intravenous pyelogram showing downward displacement of both kidneys by large abdominal mass. *B*, Inferior venacavagram shows obstruction to cephalad flow by mass and paravertebral collateral circulation.

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Figure 2 *Continued.* *C*, Stage IV-S neuroblastoma involving the entire liver found at laparotomy.

able therapy in Stage I cases. Doses of 2500 to 3500 R are employed for Stage II and III tumors in most children's centers. While there has been no objective evidence to show that one or two-drug chemotherapy has improved survival these agents have been useful in shrinking previously unresectable tumors, thus making them amenable to "second look" resection and for palliation. At present, three-drug chemotherapy is employed in patients with Stage II and III disease using Cytoxan 750 mg per m^2 on day 1, vincristine 1.5 mg per m^2 on day 5, and DTIC (imidazole carboximide) 250 mg per m^2 per day for 5 days in monthly cycles for 1 year in addition to surgery and radiation therapy. In addition, three-drug chemotherapy results in a partial or complete response to therapy in 75 per cent of Stage IV cases where survival is most unusual (2.5 per cent in collected series and none in our own experience). Infants under 1 year of age and those with Stage 1, II, and IV-S lesions have a favorable prognosis. Unfortunately, the overall survival rate is approximately 30 per cent due to the large number of dismal Stage IV cases seen.[18]

It is of interest that 1 per cent of infant autopsies (in the first 3 months of life) demonstrate neuroblastoma "in-situ" whereas the tumor presents clinically in only 1:10,000 cases. This suggests that a certain natural immunologic surveillance mechanism is protecting the host by preventing tumor growth. Recent studies concerning the immunologic aspects of this tumor show that the sera of patients with neuroblastoma contain antibodies against the tumor and that lymphocytes from patients and their relatives may destroy neuroblastoma cells grown in tissue culture. Evans et al. observed that survivors had higher peripheral

lymphocyte counts than those who died.[7] Patients who develop bone metastases demonstrate an additional antibody, a "blocking antibody" which fixes to the neuroblast and inhibits the ability of the host lymphocyte to destroy these malignant cells. Studies are presently in progress at some centers evaluating the effect of immunologic stimulants such as BCG in conjunction with high dose three-drug chemotherapy and resection of the primary tumor and bone marrow transplants at other centers in hopes of improving the duration of remission and the present dismal survival rate (2.5 per cent) in Stage IV cases.

NEPHROBLASTOMA (WILMS' TUMOR)

Nephroblastoma usually presents as a smooth, round, firm, slightly moveable flank mass that does not transilluminate. The mass is commonly noted in an otherwise asymptomatic healthy infant or child. Congenital anomalies such as hemihypertrophy and sporadic aniridia are associated with nephroblastoma and should prompt the physician to perform an intravenous pyelogram. Up to 1/3 of the patients with sporadic aniridia may have a Wilm's tumor.[9, 19] Similarly, children with neurofibromatosis, the Beckwith-Weidemann syndrome, and those with genitourinary anomalies or a family history of congenital renal anomalies are also at risk for developing nephroblastoma. Hematuria is occasionally observed as a result of involvement of the renal collecting system. Hypertension may be noted in a number of cases due to compression of the renal artery branches by tumor. In occasional cases, elevated serum renin and erythropoeitin levels have been observed.

The intravenous pyelogram remains the most effective diagnostic procedure and usually demonstrates an intrinsic distortion of the collecting system. Occasionally, the pyelogram shows nonvisualization on the side of the tumor, and calcification is rarely seen. Inferior venacavography may demonstrate extension of tumor into the vena cava from the renal vein, compression by the primary tumor or by enlarged periaortic lymph nodes. Renal arteriograms are reserved for selected cases, such as bilateral Wilms' tumor (8 to 10 per cent of cases) where evaluation of the least involved kidney for heminephrectomy is critical and in cases of hemihypertrophy with bilateral nephromegaly and calyceal distortion.

Chest x-ray is always obtained because the lung is a common site of metastases (Fig. 3). Lung tomography may confirm the presence of pulmonary metastases in questionable cases. Metastastic bone survey, bone scan, and bone marrow aspirate are usually negative. Liver scan occasionally shows involvement by direct extension from a right Wilms' tumor, rarely demonstrates metastastic lesions, and may be useful as a baseline study for evaluation of possible post-treatment "radiation hepatitis."

The therapy for nephroblastoma is often directly dependent on the stage of the disease at the time of diagnosis. Group I lesions are resectable tumors limited to the kidney without involvement of the capsule, renal vein, local para-aortic nodes, or distant spread. Operation is per-

Figure 3. Pulmonary metastases due to Wilms' tumor managed successfully by x-ray and chemotherapy without the need for operative intervention.

formed by the transperitoneal route through a long supraumbilical transverse incision large enough to carefully examine the contralateral kidney and remove the tumor without rupture. The renal vein should be isolated as promptly as possible and doubly ligated both proximally and distally to prevent possible tumor spread from the renal vein by manipulation. The procedure includes radical nephrectomy, adrenalectomy (for upper pole lesions), ureterectomy, and lymph node dissection (Fig. 4). Almost the entire length of ureter must be excised as urothelial spread has been observed. Radiation therapy is usually omitted in Group I patients under the age of 2 years. These patients are, however, treated with courses of combination chemotherapy in the form of actinomycin-D (15 μg per kg per day $\times$ 5 days per course) *and* vincristine (1.5 mg per m^2 per wk). Actinomycin-D has a significant antitumor effect and is particularly useful in the prevention of pulmonary metastases. Vincristine has also been a very effective drug in instances of Wilms' tumor. When both drugs are used in combination, the survival rate is significantly better than using either drug alone.[27] Courses of combination drug therapy are given at the time of resection, 6 weeks later, and every 3 months for a 15-month period. When radiation to the renal fossa is omitted, lymph node dissection is strongly suggested to ensure correctness in staging and to diminish the incidence of local recurrence of disease. The survival rate in Group I cases is over 90 per cent. Recent attempts to omit

Figure 4. *A*, Large left flank mass observed in a 4-year-old boy. *B*, The mass was a large Wilms' tumor which was completely encapsulated and treated successfully by combined therapy (x-ray, Actinomycin-D, and Vincristine).

radiation therapy in Group I cases over the age of 2 years have been associated with a suspicious increase in local recurrence of tumor and hepatic involvement. This suggests the continuation of radiation treatment in Group I cases over the age of 2 years.

Group II nephroblastoma refers to those cases in which the renal vein, perirenal tissues, or local lymph nodes are involved but the tumor and local tissues are completely resectable. Following the radical operation outlined above, radiation treatment is used in all age groups. The tumor field is outlined by silver clips at operation to guide the radiotherapy portal. Radiation doses ranging from 2000 to 4000 R according to the age of the patient are administered to the renal fossa. In addition, all Group II Patients receive courses of actinomycin-D (which potentiates radiotherapy) and vincristine for 15 months. Survival in Group II cases is 80 per cent.

Group III defines a lesion which is incompletely resected, only biopsied, has peritoneal implants, or is spilled by rupture of tumor at the time of attempted resection. Disease is confined to the abdomen without distant metastases. With adequate exposure through a large enough incision (which may include an intrathoracic extension), it is rare to have tumor spill. Intraoperative biopsy of Wilms' tumor should be avoided except under the most unusual circumstances (bilateral cases). Irradiation and chemotherapy as previously outlined are applied to Group III cases with the addition of adriamycin 60 mg per m^2 (total dose less than 500 mg per m^2) at 3-month intervals alternating every 6 weeks with actinomycin-D and vincristine for 15 months. Extension of tumor into the vena cava should be managed by careful vascular control, venotomy, and removal of the vena caval mass. Such cases should be carefully evaluated for possible intracardiac extension and pulmonary metastases. Utley et al. and Anselmi et al. reported successful removal of Wilms' tumor from the right atrium and pulmonary vessels using cardiopulmonary bypass.[1, 25] Prophylactic radiotherapy to the lung fields may be considered in such instances as microscopic lung metastases have probably occurred in these cases.

Group IV cases are those in which hematogenous dissemination occurs. This usually implies lung metastases (the most frequent site of spread). Metastases may also occur in brain, liver, and distant lymph nodes. Bone involvement is uncommon. Lung metastases are managed by radiation to both lung fields (1400 to 2000 R) regardless of the number and location of metastases on chest x-ray. The lung portal includes the apices and the infradiaphragmatic portions of the lung. Chemotherapy in the form of actinomycin-D, vincristine, and adriamycin is also employed. If no response is observed in 4 to 6 weeks and the tumor is isolated to one lobe or lung on laminography, thoracotomy and appropriate pulmonary resection are advocated. Recent data concerning lung metastases suggest that wedge resection may be adequate when followed by actinomycin-D and vincristine therapy.[2] Pulmonary lobectomy or pneumonectomy, however, may be required in certain instances. Survival in Group IV cases, even when lung metastases are present, is not uncommon (35 to 40 per cent).

Liver involvement by direct extension of a right Wilms' tumor is treated by nephrectomy and en bloc resection of the involved liver with expectation of survival and cure. Metastatic disease isolated to one lobe of the liver may be treated successfully by hepatic segmentectomy or lobectomy when indicated. These patients are then treated by regional radiotherapy and chemotherapy as outlined above. In those instances in which hepatic lobectomy is performed it is wise to withhold both radiation and chemotherapy for at least 3 weeks until hepatic regeneration has taken place. Both of these modalities interfere with hepatic regeneration and DNA synthesis. Doses up to 3000 R may be employed in unresectable cases where both lobes of the liver are involved over a 3 to 4 week period. Brain metastases are similarly treated. Traggis et al. recently reported successful resection of a brain metastasis with long-term survival.[23]

Using this aggressive combined therapeutic program, the overall survival rates for Wilms' tumor are approaching 80 per cent. One of the most difficult areas in the treatment of Wilms' tumor however, concerns those patients who have bilateral Wilms' tumor (8 to 10 per cent of the patients) (Group V). Two-thirds of these patients have simultaneous tumors at the initial diagnosis, while in one-third the contralateral kidney becomes involved at some time thereafter, usually within 3 to 4 years of the initial diagnosis. Total nephrectomy on one side and partial nephrectomy on the opposite side is the most frequent operation employed. About one-third of the cases survive; however, some are complicated by the development of postradiation nephritis to the remaining half of renal tissue. Recent attempts at initial bilateral biopsy, treatment with radiation and chemotherapy followed by re-exploration and appropriate nephrectomy and heminephrectomy have been successfully attempted. In addition, bench surgery and autotransplantation of the remaining half of kidney have also been attempted. Bilateral nephrectomy and subsequent renal transplantation were reported by De Lorimer et al.[5] This procedure should be reserved for cases of diffuse involvement of both kidneys. Transplantation should be considered only in those cases that do not respond to radiation therapy and combined chemotherapeutic measures. In these cases, it is probably preferable to maintain these children on long-term dialysis (2 years) prior to attempting transplantation. Immunologic suppression required to prevent allograft rejection presents a favorable situation for stimulation of persistent microscopic tumor foci and subsequent growth of metastatic disease.

LIVER TUMORS

Primary liver tumors in infancy and childhood are most commonly of hepatic cell or supporting structure origin and are occasionally mixed tumors. Two-thirds of the cases are malignant in nature and most frequently occur in the first 2 years of life. In a recent survey of 375 liver tumors conducted by the Surgical Section of the American Academy of

Pediatrics, 252 were malignant and 123 were benign.[8] Hepatoblastoma was the most common malignant tumor (129 cases), followed by hepatocarcinoma (98 cases). The former lesion occurred in the infant age group and was rarely encountered after 3 years of age. Hepatocarcinoma occurs in two age peaks in children: at 3 to 4 years of age and in teenagers between 12 and 15 years. Boys are affected slightly more frequently than girls. Epidemiologic studies of childhood liver tumors suggest that the central and Great Lakes regions of the United States have the highest incidence.[3] Hepatoblastoma has been associated with other hepatic problems including biliary atresia, neonatal hepatitis, von Gierke's disease, and the de Toni-Fanconi syndrome. In addition, co-existing extrahepatic anomalies such as hemihypertrophy and hemangiomas have also been observed. Hepatocarcinoma has also developed in patients with biliary atresia and healed hepatic histiocytosis-X and following radiation therapy for liver hemangioma. Sexual precocity due to increased gonadotropin secreted by hepatic tumors has also been noted.

Abdominal enlargement associated with an upper abdominal mass was noted in approximately 50 per cent of cases (Fig. 5*A*). The mass is usually palpable and is located in the right upper abdomen or epigastrium and moves with respiration. Pain, fever, weight loss, and anemia are frequent findings. Jaundice is seen in only 15 per cent of the cases.[8]

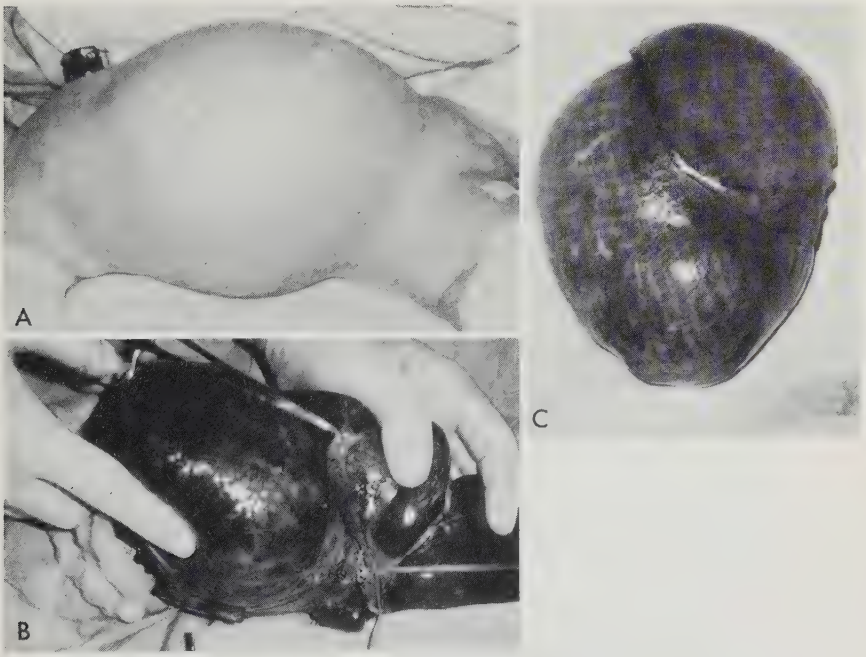

Figure 5. *A*, Five-month old infant with large upper abdominal mass. *B*, The mass was a hepatoblastoma involving the right lobe of the liver. Strictures in the portahepatis show right hepatic artery and duct and portal vein branches ligated and divided. *C*, Shows resected right lobe and tumor.

Laboratory studies are of little value in the preoperative patient evaluation. Alkaline phosphatase and SGOT levels are occasionally elevated; however, most liver function tests are essentially normal especially in the hepatocarcinoma patient. The alpha-fetoprotein was elevated in the sera of 66 per cent hepatoblastoma patients and in 40 per cent of those with hepatocarcinoma in this series.[8]

Plain x-rays of the abdomen show a right upper quadrant mass in a large number of cases (85 per cent). Hepatosplenomegaly, elevation of the right diaphragm, and pulmonary metastases (10 per cent of cases) are frequently noted findings. Inferior venacavography shows distortion or obstruction in a significant number of cases. Hepatic arteriography provides valuable information regarding the hepatic blood supply, operability, and the nature and degree of lesion vascularity. The liver scan is a useful diagnostic aid. The study was "positive" in 62 of 66 children with hepatoblastoma and all but one of 43 patients with hepatocarcinoma in the Academy Survey. The tumor appears as a "cold" space-occupying lesion.

Hepatoblastomas were located in the right lobe in 71 cases, left lobe in 20, both lobes in 38, and were multicentric in 18. In instances of hepatocarcinoma, the tumor involved both lobes in 43 cases, right lobe in 38, left lobe in 16, and was multicentric in 31. The lungs are the most common site of metastases. Other sites included intraabdominal viscera, lymph nodes, bone marrow, and brain.

Therapy of choice, when feasible, is an appropriate extirpative right or left hepatic lobectomy or extended lobectomy. Forty-five of 78 hepatoblastoma patients who had complete resection for "cure" survived (60 per cent). There were no survivors among 51 patients who had incomplete resections or biopsy alone. The overall survival rate in patients with hepatoblastoma is 35 per cent. Twelve of 36 hepatocarcinoma patients resected for cure survived (35 per cent), whereas the overall survival rate is only 13 per cent. The size of these primary tumors was often greater than 10 cm; however, tumor size does not correlate with survival.

Operative procedures have been standardized to permit the relatively safe resection of up to 85 per cent of the liver. Resections are handled in a rather uniform fashion utilizing techniques of inflow and outflow hemostasis, liver compression, and ligation of individual biliary ducts and vessels. A thoracoabdominal incision is preferred to reduce the risk of air embolism and provide easy intrapericardial access to the inferior vena cava and the hepatic veins. (Fig. 5,*B* and *C*) Appropriate monitoring techniques and two large upper extremity intravenous lines should be available for blood transfusion. Excessive blood loss is the most common complication and resulted in cardiac arrest in the operating room in eight cases and early postoperative death in 17 more in the Academy Survey.

A better understanding of segmental hepatic anatomy, a standardization of operative procedure, and a greater appreciation of the metabolic and physiologic considerations that follow hepatic resection have improved the survival. Appropriate glucose infusion, albumin replace-

ment, and vitamin-K administration are given for the first 4 to 5 postoperative days. Hemihepatectomy, however, is not without its risks; 25 and 33 per cent operative mortality rates have been reported.[3]

There is no objective evidence to show that radiation and chemotherapy result in cures in instances where the tumor could not be completely excised. The greatest role for these ancillary treatment modalities appears to be in patients with hepatoblastoma who are originally thought to have an unresectable tumor and become operable at a "second look" procedure after responding to x-ray and combined chemotherapy (actinomycin-D, vincristine, and Cytoxan). Hermann and Lonsdale[16] and Hasegawa et al.[13] documented such occurrences. An additional role for such adjunctive therapy is in those cases with tumor "spill" or rupture at the time of attempted resection.

Randolph* proposed a treatment protocol according to the stages of disease:

Group I Localized tumor completely resected; hepatic resection with no further therapy.

Group II–A Localized tumor, treated by x-ray and chemotherapy (Cytoxan, vincristine, and Adriamycin), which is rendered completely resectable.

Group II–B Incomplete resection with localized residual disease; x-ray plus triple-drug chemotherapy.

Group II–C Localized tumor with biopsy alone and no attempt at resection; x-ray and triple-drug therapy.

Group III Tumor involving both lobes of liver; biopsy, x-ray to whole liver, and triple-drug chemotherapy.

Group IV Metastatic disease; triple-drug chemotherapy.

RHABDOMYOSARCOMA

Rhabdomyosarcoma in children is a highly malignant tumor with a tendency to early recurrence and eventual distant metastases. This neoplasm represents 10 to 15 per cent of all childhood malignant solid tumors. The most frequent sites of occurrence in adults are the trunk and extremities. In children, however, the tumor originates in the head and neck in 28 per cent of cases, orbit 11 per cent, trunk 33 per cent, extremities 15 per cent, and pelvis and perineal areas 13 per cent (Fig. 6). Occasionally, primary sites may involve a bronchus, the common bile duct, retroperitoneal space, middle ear, the sinuses, and paratesticular areas (Fig. 7).

Clinical presentation is usually that of a mass in the neck, extremities, perineum, and buttocks areas (Fig. 8). Bladder tumors often arise at the trigone or bladder base and present with hematuria, frequency, urinary incontinence, and progressive urinary obstruction. More rarely, the dome of the bladder or the prostrate is the site of occurrence. Vaginal lesions usually arise on the anterior wall near the urethra and present with bloody vaginal discharge or prolapse of a polypoid tumor. The tumors often assume a botryoid (grape-like clusters) appearance

*J. G. Randolph, personal communication.

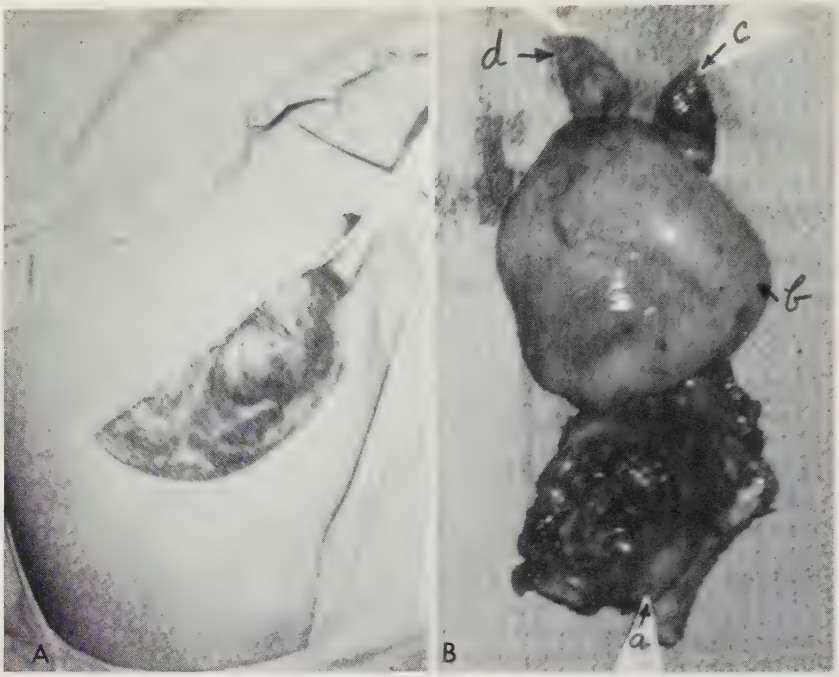

Figure 6. *A*, Chest wall rhabdomyosarcoma involving the intercostal muscles in a 9-year old girl. *B*, An en bloc dissection included the chest wall (*a*), the mass which extended into mediastinum (*b*), and was adherent to the right upper lobe (*c*) and right middle lobe (*d*) of the lung The involved segments of pulmonary tissue were wedge resected with the mass.

within pelvic organs (bladder, vagina, uterus) and the common bile duct. The latter cases often present with obstructive jaundice. Orbital lesions may present with a "black eye," proptosis, and exophthalmus much like a neuroblastoma or retinoblastoma.

Preoperative evaluation includes a complete blood count, urinalysis, platelet count, chest x-ray and tomography, skeletal survey, bone scan, liver scan, and intravenous pyelogram. For head and neck lesions, direct and indirect laryngoscopy, otologic and ophthalmologic examination, brain scan, and evaluation of cerebrospinal fluid for presence of tumor cells are performed. Cystoscopy, vaginoscopy, and voiding cystourethrogram and low segment barium enema are done for pelvic lesions. Gallium scan, lymphangiogram, and venacavography are performed for paratesticular and retroperitoneal lesions.

Therapy is administered according to appropriate clinical staging designed by the National Intergroup Rhabdomyosarcoma Study.

Group I lesions denote completely resected localized disease confined to the muscle or organ of origin. These cases are treated with radiation therapy (regional) and three-drug chemotherapy in the form of actinomycin-D (15 μg per kg per day), vincristine (2 mg per kg per wk), and cyclophosphamide (2.5 mg per kg per day) in cyclic courses for 2 years. More recently, some institutions are omitting radiation in Group I patients.

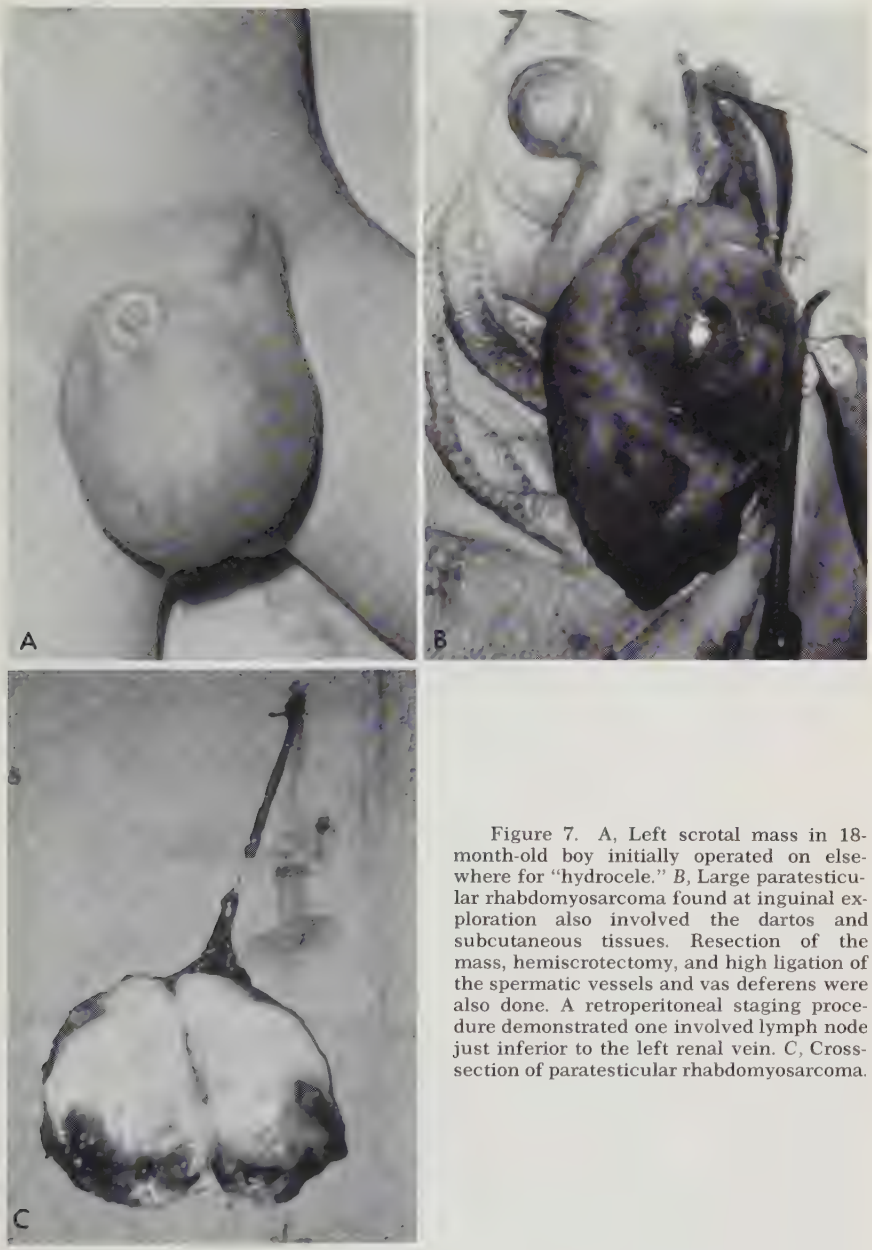

Figure 7. A, Left scrotal mass in 18-month-old boy initially operated on elsewhere for "hydrocele." *B*, Large paratesticular rhabdomyosarcoma found at inguinal exploration also involved the dartos and subcutaneous tissues. Resection of the mass, hemiscrotectomy, and high ligation of the spermatic vessels and vas deferens were also done. A retroperitoneal staging procedure demonstrated one involved lymph node just inferior to the left renal vein. *C*, Cross-section of paratesticular rhabdomyosarcoma.

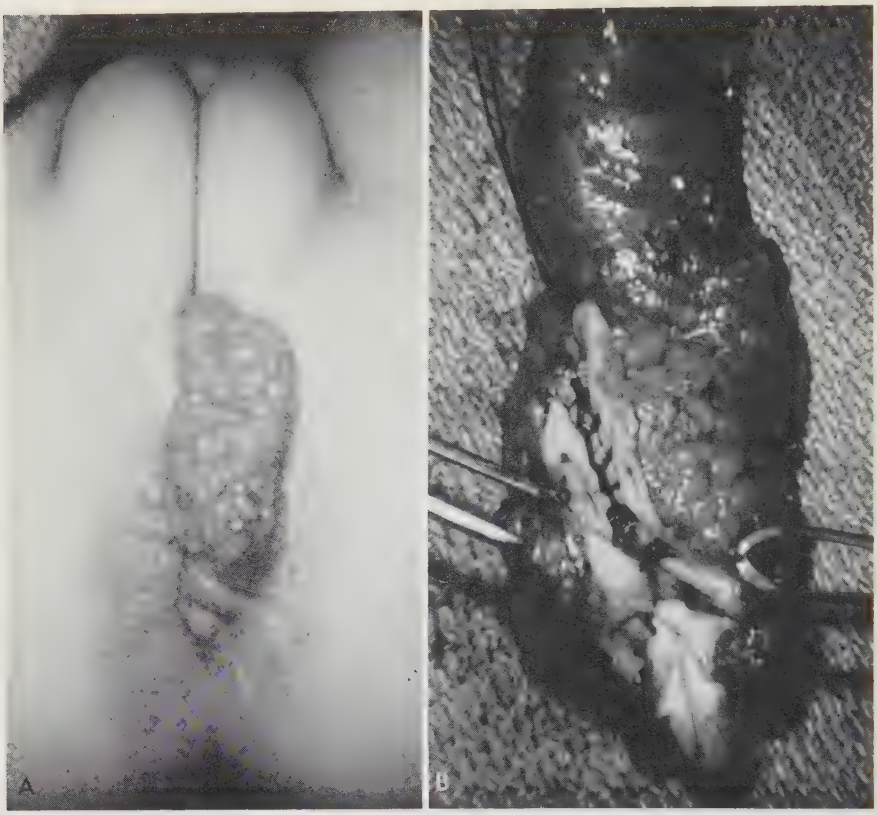

Figure 8. *A*, Perianal embryonal rhabdomyosarcoma in the three-month-old girl. *B*, The lesion involved the external sphincter muscle. An abdominoperineal resection was performed.

Group II includes three subgroups of patients:

IIa: Grossly resected tumor with microscopic residual disease and negative lymph nodes.

IIb: Regional disease with extension into adjacent organs and with positive nodes; completely resected and with no microscopic residual.

IIc: Regional disease with both positive nodes and microscopic residual disease.

All three subgroups receive regional x-ray therapy, actinomycin-D, and vincristine over a 2-year period.

Group III involves patients with incomplete resection and gross residual disease or biopsy only. These patients are initially treated with simultaneous actinomycin-D, vincristine, and Cytoxan (10 mg per kg per day) to reduce tumor size; x-ray treatment is initiated 6 weeks later. Adriamycin (60 mg per m^2) is also employed.

Group IV involves patients with distant metastases present at the onset (lung, liver, bone, bone marrow, brain, distant lymph nodes). Treatment is similar to that outlined for Group III Cases.

Radiation therapy in cases of rhabdomyosarcoma involves large doses in the range of 5000 to 6000 R except in children under the age of 3 years where 4000 R is maximum. Tissue sparing to special organs is also considered so therapy does not exceed 1800 R to both lungs, 1500 to 2000 R to the kidneys, and 3000 R to the liver.

Prior to 1967, the survival rate in childhood rhabdomyosarcoma was 14 per cent. Since the initiation of aggressive combined therapy, a dramatic improvement in survival has been observed.[12] Most (90 per cent) Group I Patients are alive and free of disease. A 70 per cent survival rate is achieved in Group II patients and 35–40 per cent for Group III. While significant palliation has been achieved in Group IV cases, these patients still have a relatively poor prognosis (10 per cent survival). More than 60 per cent of cases are Group III or IV at the time of initial diagnosis, yet the overall survival in some centers approaches 70 per cent.[17]

Due to the improvement in results achieved with combined treatment, surgical guidelines for these tumors have changed from what was previously considered traditional extirpative cancer procedures. In instances of orbital rhabdomyosarcoma, radiation therapy following biopsy appears to be as acceptable a treatment as orbital exenteration. In many children's centers, extremity lesions have been successfully treated by local resection, x-ray, and multi-drug chemotherapy rather than resorting to amputation. In instances of pelvic rhabdomyosarcoma, total exenteration is no longer the therapy of choice in the majority of cases. Simple hysterectomy or occasionally anterior pelvic exenteration with rectal preservation following combined modality treatment has been successful in many cases. If the tumor is grossly resected, microscopic residual tumor can probably be controlled by adjunctive measures. Even in instances of local recurrence of disease, secondary local resection , occasionally amputation followed by further cyclic chemotherapy, has resulted in some cures. Formal elective lymph node dissections are not considered a routine addition to every local resection. In instances of pelvic and paratesticular lesions, however, evaluation of iliac and retroperitoneal lymph nodes appears to be beneficial particularly for staging purposes.

TERATOMAS

Teratomas are embryonic neoplasms containing all three germ layers (ectoderm, mesoderm, and endoderm) derived from toti-potential cells. These lesions occur in the midline or paramedian plane from the brain to the sacrococcygeal area. In 68 children observed at the James Whitcomb Riley Hospital for Children, tumor location was paratracheal (3), anterior mediastinal (10), retroperitoneal (2), gonadal (8), presacral (3), and sacrococcygeal (43). Tumors were significantly more frequent in girls (2:1) (Fig. 9). The majority of cases are recognized in the neonatal period or early childhood. A family history for twinning was noted in 10 per cent of cases. Eighty per cent of the lesions are benign and 20 per cent malignant. Both benign and malignant tumors were frequently calcified (35 per cent).

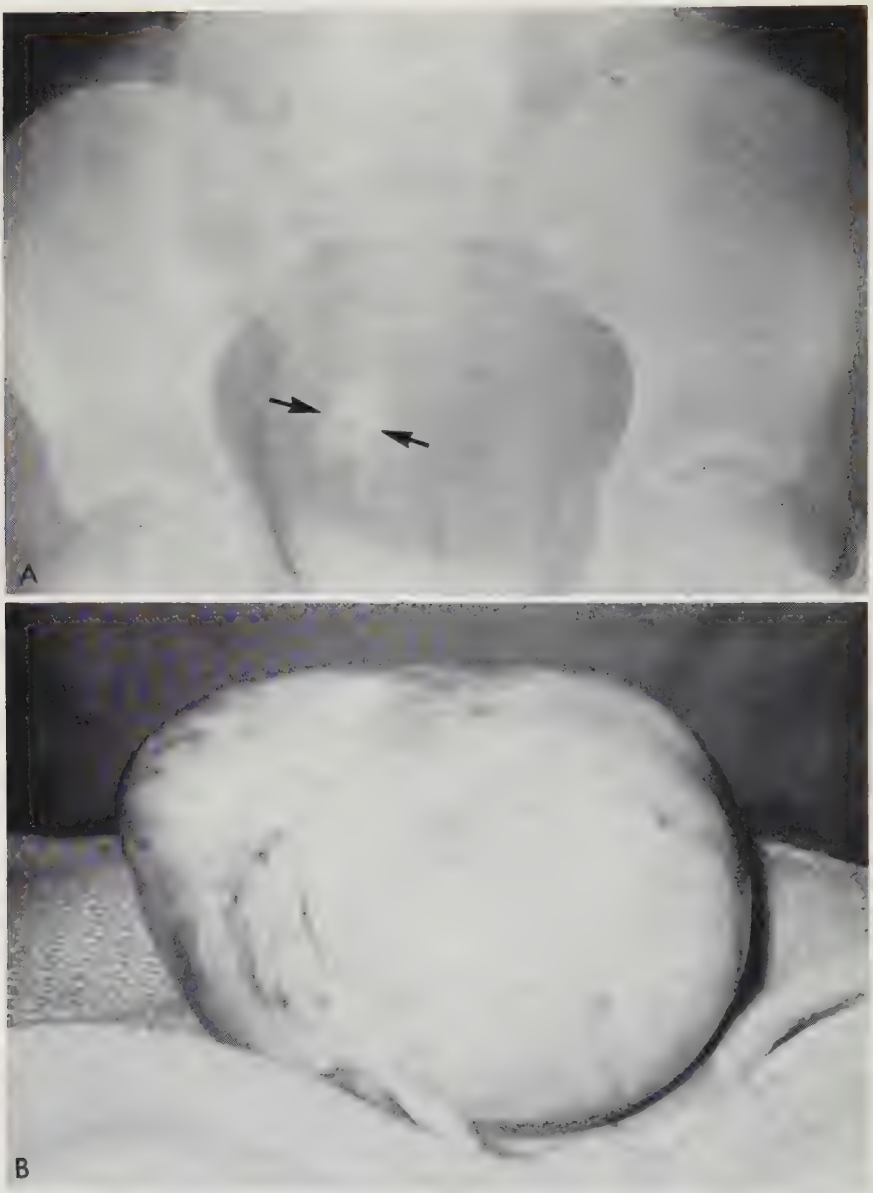

Figure 9. *A*, X-ray of the abdomen of a 9-year-old girl with a palpable lower abdominal mass shows calcification *(arrows)* in the mass. *B*, Large ovarian teratoma found and excised at operation.

Teratomas have a definite tendency toward malignant degeneration particularly after the age of 3 months. Sera from patients with malignant lesions are usually positive for alpha-fetoprotein, probably of yolk sac origin.[24] Gitlin et al. observed that large amounts of alpha-fetoprotein are synthesized by the fetal liver and the yolk sac during early embryonic life.[10] Many malignant teratomas are endodermal sinus tumors that resemble a rat yolk sac. The observations from patients and their sera containing alpha-fetoprotein strongly suggest that these malignant tumors are indeed of yolk sac origin. Sera from most infants with benign teratomas are usually negative for alpha-fetoprotein, especially after the first month of life.

Most sacrococcygeal teratomas present in the neonatal period. Careful inspection of the sacral area perineum and buttocks should be a part of every newborn examination. Rectal examination may reveal a presacral mass. Tumors are cystic, solid, or a mixture (Fig. 10). The incidence of malignancy is rare in the newborn (7 per cent), but rapidly increases after 3 months. This stresses the need for early operative resection usually performed in the first week of life. Operation is accomplished by the sacral approach with the patient in a "jack-knife" position. Appropriate monitoring and a reliable intravenous infusion route for blood transfusion are mandatory. Careful control of the prominent midsacral vessels that often supply these tumors is essential and may significantly minimize blood loss during operation. The major complication observed in these cases is hemorrhage. In almost every instance, the levators and external sphincter muscles can be preserved. A chevron incision is usually employed; however, modifications are made in selected cases. In 10 to 15 per cent of cases, the tumor may extend up through the pelvic inlet into the abdomen and a combined abdominosacral resection is required for excision.[15] The coccyx should be removed with the tumor, as failure to do so results in recurrence of tumor in 35 per cent of cases.

Malignant lesions metastasize to liver, lungs, bone marrow, and brain, and may extend locally into the sacrum and pelvis. We have observed a good response to adjunctive therapy (x-ray and chemotherapy) in five patients with malignant tumors, including one testicular, one ovarian, and three sacrococcygeal teratomas. X-ray doses of 3500 to 4000 R followed by combination chemotherapy using actinomycin-D, vincristine, methotrexate, and Cytoxan has reduced the size of tumors previously considered irresectable and allowed a "second look" resection. Lung metastases have similarly responded by decreasing in size and have been successfully excised at thoracotomy. These observations suggest a more aggressive role for these adjunctive measures in cases of malignant teratomas.

COMPLICATIONS OF CANCER THERAPY

The use of aggressive combined modality treatment has unquestionably improved the survival of children with embryonal malignancies. The administration of irradiation therapy and anti-tumor drugs is not innocuous, however.

Figure 10. *A*, Huge sacrococcygeal tumor observed in an 8 pound, three-day-old girl. *B*, The resected tumor weighed 3 pounds.

Irradiation may result in tissue inflammation and destruction, parenchymal aging, scoliosis, dermatitis, radiation nephritis, pneumonitis, and radiation hepatitis. Growth retardation from epiphyseal radiation is occasionally encountered. Pelvic irradiation may cause significant radiation (actinic) cystitis and proctocolitis. The use of a 250 KV source has a greater tissue damaging effect than the less often used ^{60}C. source. The morbidity of irradiation therapy is significantly increased by concomitant use of radiation enhancing drugs including actinomycin-D, adriamycin, and high-dose cyclophosphamide. Careful evaluation of dosage schedules and treatment portal by radiotherapists with considerable experience in the management of pediatric neoplasms is strongly suggested.

In addition, second malignant neoplasms (leukemia, osteogenic sarcoma, chondrosarcoma, soft tissue sarcomas, squamous cell carcinoma, etc.) have also been observed in long-term survivors (2.5 per cent) following irradiation treatment. Sixty per cent of these cases occur within the actual radiation portal. The median time of occurrence is 8 years post-treatment.*

Complications of chemotherapy are of two types: (1) those related to the drug itself, and (2) in the form of a potentially fatal infection as a consequence of immune suppression. Some complications may be avoided by proper dose scheduling while other forms are unpredictable.

Cyclophosphamide is associated with hemorrhagic cystitis which may progress to severe hemorrhage, a scarred contracted bladder, and an increased risk of bladder carcinoma.[26] The incidence of hemorrhagic cystitis is increased if concomitant x-ray therapy or high dose cyclophosphamide is given. Appropriate hydration and administration of diuretics is suggested if hematuria is observed. Anemia, leukopenia, thrombocytopenia, nausea and vomiting are also frequently seen with cyclophosphamide treatment. Alopecia is common; wigs are of great value for adolescent patients. Azospermia is also observed; however, few data are available concerning long-term effects.

Vincristine therapy is associated with neurotoxicity manifested by peripheral neuritis ("toe walking"), loss of deep tendon reflexes, ptosis, and facial and extremity paresis. Paresthesias and difficulty with fine motor movements are other manifestations of central nervous system problems. Adynamic ileus, constipation, and abdominal pain that may mimic appendicitis are observed in 1/3 of the children treated with vincristine. Jaw pain is also noted in some patients.

Actinomycin-D causes thrombocytopenia, leukopenia, nausea, vomiting, diarrhea, and oral mucosal ulcerations. It is a very irritating agent and causes severe skin and subcutaneous tissue slough if infiltration occurs. Actinomycin-D potentiates x-ray therapy, but seems to have a protective effect against the occurrence of a second malignancy within the irradiation fields. Actinomycin-D acts on the active mitotic phase of cell turnover and can inhibit hepatic regeneration when used early in the posthepatic lobectomy course.

*G. J. D'Angio, personal communication

Adriamycin causes irritation, neutropenia, thrombocytopenia, alopecia, and in addition may result in cardiotoxicity when the cumulative dose is over 550 mg per m^2. This may or may not be heralded by the occurrence of arrhythmias and electrocardiographic changes which, when present, demand rapid cessation of therapy. These changes have been noted at lower cumulative doses when irradiation of the chest is also given. Congestive heart failure may follow rapidly and often is unamenable to therapy and proves fatal. Adriamycin, like actinomycin, potentiates irradiation therapy, but also appears to potentiate BCG immunostimulation. Adriamycin is very potent in infants and in some centers is not employed in patients in the first year of life.

Methotrexate can result in oral and gastrointestinal ulceration as well as long-term complications such as hepatic damage (fibrosis) and pulmonary fibrosis. Severe central nervous system toxicity in the form of encephalopathy has been observed, particularly when CNS x-ray and methotrexate therapy are used simultaneously.

Immunologic suppression occurs more frequently when combination chemotherapy is employed, especially with high-dose Cyclophosphamide and Adriamycin. Severe neutropenia may result in instances of overwhelming bacterial infection. When febrile, these patients at risk must be treated both aggressively and rapidly with antibiotic (oxacillin, gentamycin, and carbenicillin) therapy. Depression of delayed hypersensitivity responses results in instances of overwhelming viral (cytomegalic inclusion disease, herpes simplex, zoster-varicella), protozoan (pneumocystis carinii), and fungal infections. These must also be recognized and treated with zoster immunoglobulin, pentamadine, amphotericin-D, and the like as indicated.

These complications strongly emphasize the need for such patients to be managed in an appropriate pediatric cancer facility capable of recognizing, identifying, and treating a wide variety of infections in children with solid tumors on combined immunosuppressive chemotherapy.

REFERENCES

1. Anselmi, G., Suarez, J. A., Machado, I., et al.: Wilms' tumor propagated through the inferior vena cava in the right heart cavities. Br. Heart J., *32*:575, 1970.
2. Ballantine, T. V. N., Wiseman, N. E., and Filler, R. M.: Assessment of pulmonary wedge resection for the treatment of lung metastases. J. Ped. Surg., *10*:671, 1975.
3. Clatworthy, H. W., Jr., Schiller, M., and Grosfeld, J. L.: Primary liver tumors in infancy and childhood. Arch. Surg., *109*:143, 1974.
4. D'Angio, G. J., Evans, A. E., and Koop, C. E.: Special pattern of widespread neuroblastoma with a favourable prognosis. Lancet, *1*:1046, 1971.
5. deLorimier, A. A., Belzer, F. O., Kountz, S. L., and Krishner, J. H.: Simultaneous bilateral nephrectomy and renal allotransplantation for bilateral Wilms' tumor. Surgery, *64*:850, 1968.
6. Evans, A. E., D'Angio, G. J., and Randolph, J. G.: A proposed staging for children with neuroblastoma. Cancer, *27*:374, 1971.
7. Evans, A., Albo, V., D'Angio, G., et al.: Factors influencing survival of children with nonmetastatic neuroblastoma. Cancer (in press).
8. Exelby, P. R., Filler, R. M., and Grosfeld, J. L.: Liver tumors in children in the particular reference to hepatoblastoma and hepatocellular carcinoma: American Academy of Pediatrics, Surgical Section Survey, 1974. J. Ped. Surg., *10*:329, 1975.

9. Fraumeni, J. F., Jr., and Glass, A. G.: Wilms' tumor and congenital aniridia. J.A.M.A., *206*:825, 1968.
10. Gitlin, D.: Sites of alpha-fetoprotein synthesis. N. Eng. J. Med., 285:1436, 1971.
11. Grosfeld, J. L., and Baehner, R. L.: Role of combined therapy in childhood solid tumors. Paediatrician, 3:271, 1974.
12. Grosfeld, J. L., Clatworthy, H. W., Jr., and Newton, W. A., Jr.: Combined therapy in childhood rhabdomyosarcoma: An analysis of 42 cases. J. Ped. Surg. *4*:637, 1969
13. Hasegawa, H., et al.: Embryonal carcinoma and alpha-fetoprotein with special reference to hepatoblastoma. Gann, *14*:129, 1973.
14. Hellstrom, I., Hellstrom, K. E., and Bill, A. H., et al.: Studies in cellular immunity to human neuroblastoma cells. Int. J. Cancer, 6:172, 1970.
15. Hendren, W. H., and Henderson, B. M.: The surgical management of sacrococcygeal teratomas with intrapelvic extension. Ann. Surg., *171*:77, 1970.
16. Hermann, R. E., and Lonsdale, D.: Chemotherapy, radiotherapy, and hepatic lobectomy for hepatoblastoma in infants: Report of a survival. Surgery, *68*:383, 1970.
17. Kilman, J. W., Clatworthy, H. W., Jr., Newton, W. A., Jr., and Grosfeld, J. L.: Reasonable surgery for rhabdomyosarcoma. Ann. Surg., *178*:346, 1973.
18. Koop, C. E., and Johnson, D. G.: Neuroblastoma: An assessment of therapy in reference to staging. J. Ped. Surg., 6:595, 1971.
19. Pilling, G. P.: Wilms' tumor in seven children with congenital aniridia. J. Ped. Surg., *10*:87, 1975.
20. Roberts, K. B., and Freeman, J. M.: Cerebral ataxia and "occult" neuroblastoma without opsoclonus. Pediatrics, 56:464, 1975.
21. Schnaufer, L., and Koop, C. E.: Silastic abdominal pouch for temporary hepatomegaly in Stage IV-S neuroblastoma. J. Ped. Surg., *10*:73, 1975.
22. Senelick, R. C., Bray, P. F., Lahey, M. E., and Johnson, D. G.: Neuroblastoma and myoclonic encephalopathy: Two cases and a review of the literature. J. Ped. Surg., *8*:623, 1973.
23. Traggis, D., Jaffe, N., Tefft, M., and Vawter, G.: Successful treatment of Wilms' tumor with intracranial metastases. Pediatrics, 56:472, 1975.
24. Tsuchida, Y., Urano, Y., Endo, Y., Ohmi, K., et al.: A study on alpha-fetoprotein and endodermal sinus tumor. J. Ped. Surg., *10*:501, 1975.
25. Utley, J. R., Mobin-Uddin, K., Segnitz, R. H., et al.: Acute obstruction of tricuspid valve by Wilms' tumor. Surgery, 66:626, 1973.
26. Wall, R. L., and Clausen, K. P.: Carcinoma of the urinary bladder in patients receiving cyclophosphamide. N. Eng. J. Med., 293:271, 1975.
27. Wolff, J. A.: Advances in the treatment of Wilms' tumor. Cancer, 35:901, 1975.

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